

## Supplementary Tables

**Supplementary Table 1:** List of genes that are profiled by the seqFISH experiment.

4931431F19Rik	Ctla4	Hnf1a	Obsl1	Cpne5
4932429P05Rik	Cyp2c70	Hoxb3	Olr1	Nes
Abca15	Cyp2j5	Hoxb8	Osr2	Acta2
Abca9	Dbx1	Hyal5	Pld1	Gja1
Adcy4	Dcstamp	Kif16b	Pld5	Omg
Aldh3b2	Ddb2	Laptm5	Poln	Nov
Ankle1	Egln3	Lefty2	Ppp1r3b	Col5a1
Ano7	Fam69c	Lhx3	Psmd5	Dcx
Anxa9	Fbl11	Lhx4	Rbm31y	Itpr2
Arhgef26	Foxa1	Lmod1	Rrm2	Rhob
B3gat2	Foxa2	Mertk	Scml2	Sox2
Barhl1	Foxd1	Mgam	Senp1	Cldn5
Bcl2l14	Foxd4	Mmgt1	Serpinb11	Mrc1
Blzf1	Galnt3	Mmp8	Sis	Tbr1
Bmpr1b	Gata6	Mrgprb1	Slc4a8	Pax6
Capn13	Gdf2	Murc	Slc6a16	Calb1
Cdc5l	Gdf5	Nell1	Spag6	Gda
Cdc6	Gm15688	Neurod4	Sumf2	Slc5a7
Cdh1	Gm6377	Neurog1	Tnfrsf1b	Sema3e
Cecr2	Gm805	Nfkb2	Vmn1r65	Mfge8
Cilp	Gpc4	Nfkbiz	Vps13c	Lyve1
Clec5a	Gpr114	Nhlh1	Wrn	Loxl1
Creb1	Gykl1	Nkd2	Zfp182	Slco1c1
Creb3l1	Hdx	Nlrp12	Zfp715	Amigo2

Csf2rb2	Hn1l	Npy2r	Zfp90	Kcnip2
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**Supplementary Table 2:** List of 43 genes used for cell type mapping.

Fbl1	Itpr2	Vps13c	Tnfrsf1b	Sox2
Hdx	Wrn	Sumf2	Vmn1r65	Rhob
Mrgprb1	Calb1	Pld1	Laptm5	Tbr1
Slc5a7	Abca9	Ankle1	Olr1	
Cecr2	Cpne5	Blzf1	Mertk	
Nell1	Npy2r	Cdc5l	Slco1c1	
Pax6	Cldn5	Cyp2j5	Mfge8	
Col5a1	Bmpr1b	Rrm2	Gja1	
Dcx	Spag6	Csf2rb2	Gda	
Arhgef26	Slc4a8	Gm805	Omg	

**Supplementary Table 3:** Astrocyte prediction accuracy, evaluated using fluorescent staining images. We examined and contrasted DAPI, Nissl staining on astrocyte cells. Percentage of cells with no Nissl, and with DAPI staining are recorded (these are accurate instances)

	% predicted astrocytes with weak or no Nissl stain	% predicted astrocytes with present Nissl stain	Total predicted astrocytes
Cortex Column 1	100%	0%	11
Cortex Column 2	88%	12%	25
Cortex Column 3	87%	13%	24
Cortex Column 4	87%	13%	24

**Supplementary Table 4:** List of 69 genes used for HMRF.

Calb1	Gdf5	Rbm31y	Zfp182	Pld5
Kcnip2	Nkd2	Creb3l1	Gpc4	Gm805
Tbr1	Fam69c	Nfkbid	Obsl1	Clec5a
Nes	Sema3e	Hoxb8	Dcstamp	Serpinb11
Gda	Dcx	Adcy4	Poln	Zfp715

Col5a1	Lhx3	Mmgt1	Cdh1	Blzf1
Loxl1	Omg	Lhx4	Ppp1r3b	Bm6377
Sox2	Wrn	Lefty2	Mgam	Zfp90
Slc5a7	Aldh3b2	Gm15688	Hn1l	
Nov	Foxd1	Kif16b	Hdx	
Cpne5	Cyp2c70	Vmn1r65	Psmd5	
Mrc1	Hnf1a	Foxa2	Bcl2l14	
Acta2	Slc4a8	Gpr114	Osr2	
Cyp2j5	Barhl1	Gata6	4931431F19Rik	
Lyve1	Egln3	Nhlh1	Lmod1	

**Supplementary Table 5:** Expanded domain specific signatures used for Tasic et al reanalysis

O1	gata6 aldh3b2 kcnips gm805 b3gat2 amigo2 cdc6
O2	serpinb11 fam69c capn13 ankle1 mmp8 cecr2 foxd4 barhl1
O3	lmod1 mmgt1 lefty2 hn1l foxd1 pld1 olr1
O4	lhx3 omg arhgef26
I5	adcy4 nkd2 cyp2j5 dbx1 zfp715 mgam senp1 hnf1a ddb2 nfkb2 blzf1
I2	hn1l cdc5l murc nhlh1 creb1
I3	gata6 vmn1r65 sema3e foxa1 obsl1
I1a	loxl1 clec5a cpne5 creb3l1 gpc4 calb1 sox2 nes vps13c
I1b	mrc1 nkd2 sema3e col5a1 dcx slc5a7 nov rhob pax6

## Supplementary Figures

**Supplementary Fig 1:** Quantile-quantile plot per gene for 113 genes shared between seqFISH and scRNAseq data sets. Q-Q plot shows the comparison of quantiles between scRNAseq (y-axis, across n=1723 cells) and seqFISH (x-axis, across n=1597 cells). Quantiles refer to expression z-score quantiles after each scRNAseq and seqFISH has been transformed by row- and column-wise z-score normalization.

**Supplementary Fig 2:** Robustness analysis of domain identifications by HMRF model with respect to cell-type marker filtering. (a) Different scenarios. “ct” denotes “cell-type”. “Plus.11.ct.genes” denotes unfiltered scenario which added all 11 ct genes. (b, c) Agreement between domain assignment using different cell-type filtering settings. Agreement quantified by (b) overall clustering consistency and (c) contingency table. (d) Spatial patterns found by HMRF in each scenario, in comparison with 69-gene HMRF. For each scenario, the HMRF model used 1,000 initial centroids to select the best one to initiate HMRF. HMRF clustering was repeated for two more times with similar results.

**Supplementary Fig 3:** Comparison between the (a) spatial domain annotation and (b) major cell type annotation for all 1597 cells in the seqFISH data set. tSNE constructed from the 69 genes used in HMRF for the seqFISH dataset.

**Supplementary Fig 4:** Enrichment of cell types in spatial domains. Enrichment is calculated as (num. cells) / sqrt(column x rowsum), where number of cells refers to cells that overlap between a domain and a cell type. Col- and row-sums refer to the overlap table.

**Supplementary Fig 5:** Spatial expression of domain marker genes. Representative genes of the 9 domains include Barhl1 (O2), Nfkb2 (IS), Col5a1 (I1a), Aldh3b2 (O1), Calb1 (I1b), Omg (O4), Nhlh1 (I2), Gata6 (I3), and Plid1 (O3). Black outlines around some cells highlight the domain annotations. One mouse brain was assayed by seqFISH due to experimental cost.

**Supplementary Fig 6:** General domain signatures transcend cell types. For cells annotated to each cell type : spatial domain pair; only those containing at least 4 cells are represented. Top row: domain type; 2nd row: cell type. The heatmap below shows the average level of domain associated genes.

**Supplementary Fig 7:** Distribution of expression levels representative of domain- and cell-type specific marker genes. (a) Representative domain-specific marker genes. The corresponding domains are indicated in parentheses in title. (b) Representative cell-type specific marker genes. The corresponding cell types are indicated in parentheses in title. Each box represents the distribution associated with the intersection of a specific cell type and spatial domain pair. A dot inside each box represents a cell. Only pairs which contain >5 cells are analyzed, and other pairs are discarded. Boxes show the quartiles of data points with whiskers extended to show the rest of distribution. Sample sizes from left to right: n=6, 60, 11, 86, 21, 13, 71, 74, 9, 11, 8, 6, 71, 29, 93, 30, 8, 77, 78, 83, 22, 13, 171, 202, 20, 134, and 111 cells.

**Supplementary Fig 8:** Comparison of seqFISH's domain specific genes with Allen Brain Atlas. Genes compared are: Calb1, Sema3e, Gda, Nell1, Tbr1, Cpne5, Gdf5, Nov, Aldh3b2, Nkd2, Serpinb11. For each gene, the left image is the seqFISH profile ( $n=1597$  cells); the top right image shows the Allen Brain Atlas ISH staining. Bottom right shows the z-scored expression in microdissection cell clusters from Zeisel *et al* and Tasic *et al* scRNASeq data sets. SeqFISH profiles agree well with existing resources.

**Supplementary Fig 9:** Metagene expression levels. (a) 9 metagenes each marking a different spatial domain. (b) the spatial domain annotations. Metagene expression is defined as the average of general domain signature genes (Fig 2d). One mouse brain was assayed by seqFISH due to experimental cost.

**Supplementary Fig 10:** Applications of domain metagene signatures on mapping the domain patterns of glutamatergic cells. Shown are glutamatergic cells only. Red indicates metagene expression. For mapping glutamatergic cells, the expanded domain specific signatures (Supplementary Table 5) were used. This has been indicated in the legend.

**Supplementary Fig 11:** A zoom-in view of comparison between spatial domain annotations (left) and metagene expression levels (right) at domain boundaries indicated in Fig 3b. Five snapshot regions were selected to show that (meta)gene expression switching is frequently observed at domain boundaries.

**Supplementary Fig 12:** Comparison of morphological features across different spatial domains. 6 of the 15 morphological features extracted from Nissl staining images are significantly different across domains. Significance is judged by both of the following criteria, whereby 1) each domain is compared to an individual domain and is  $P<0.05$  in at least 7 of 8 one-vs-one K-S tests, and 2) each domain is compared to all cells in remaining domains ( $P<0.00001$ , one-vs-rest test). (a) The distribution of the 6 significant features across domains. (b) The P-values obtained from the one-vs-rest tests. Domains being compared have the following cell numbers: O2 ( $n=109$ ), I1a ( $n=389$ ), O4 ( $n=120$ ), I1b ( $n=79$ ), O1 ( $n=135$ ), I2 ( $n=117$ ), I3 ( $n=205$ ), O3 ( $n=270$ ), and IS ( $n=173$ ).

**Supplementary Fig 13:** ISH validation of additional spatial domain markers identified from integrative analysis. ISH images were obtained from the Allen Brain Atlas. Each gene wasa selected based on co-expression with the domain specific signatures. The ISH images shown were representative sagittal brain slices cropped to the visual cortex region. There are at least two replicates in each case.

**Supplementary Fig 14:** Overlap between spatial domain and glutamatergic subtype annotations for theTasic *et al* dataset. (a) Overlap between domain- and cell subtype-specific genes focused within the 125-gene fraction. (b) Overlap between cells annotated as a specific domain vs subtype. P-values were obtained by using the hypergeometric tests corrected for

multiple hypotheses. Cell numbers contained in each glutamatergic cell subtype are: L2/3\_Ptgs2 (n=96), L2\_Ngb (n=21), L4\_Arf5 (n=44), L4\_Ctxn3 (n=79), L4\_Scnn1a (n=99), L5\_Chrona6 (n=11), L5\_Ucma (n=16), L5a\_Batf3 (n=66), L5a\_Hsd11b1 (n=53), L5a\_Tcerg1l (n=35), L5b\_Cdh13 (n=42), L5b\_Tph2 (n=32), L5a\_Car12 (n=22), L6a\_Mgp (n=53), L6a\_Sla (n=74), L6a\_Syt17 (n=15), L6b\_Rgs12 (n=15), and L6b\_Serpib11 (n=20). Cell numbers contained in each metagene-derived cluster are: O2 (n=132), I1a (n=98), O4 (n=92), I1b (n=131), O1 (n=84), I2 (n=22), I3 (n=97), O3 (n=100), IS (n=56).

**Supplementary Fig 15:** Comparison of cell subtype annotations and metagene cluster annotations on Tasic *et al* glutamatergic cells (n=812). t-SNE plot has been generated based on metagene expression (same configuration as in Fig 4a). (a) Cell subtype annotations as provided by Tasic *et al*. (b) Metagene-cluster annotations (domains).

**Supplementary Fig 16:** Comparison of metagene-recovered spatial populations with cell subtypes in Tasic *et al* data set (n=812 glutamatergic cells). (a) Overlay of expression patterns of representative cell subtype markers (col5a1, cpne5, sema3e, serpib11) on t-SNE plot that was generated in the same way as Fig 4a (obtained from metagene signatures). Red demarcates cells expressing the gene. It can be seen that these genes served as markers of both cell subtypes and domains. (b) Some distinct populations recovered by metagenes do not correspond to any specific cell subtypes identified by Tasic *et al*. Shown are three examples (O1, I2, and O4). The second row shows the subtype annotations.

**Supplementary Fig 17:** Expression of astrocyte-associated domain genes in an external astrocyte expression database (Zhang *et al* 2016). Low-level expression is defined as <10 FPKM. High level is between 10 and 160 FPKM.

**Supplementary Fig 18:** Spatial organization of the mouse olfactory bulb as revealed by the HMRF model. (a) This spatial transcriptome data set (n=282 wells) was generated by Stahl *et al* 2016. and obtained by using tissue microarray to barcode spatial locations at a 100um resolution followed by RNA sequencing. (b) Spatial domains identified by using a 5-state HMRF model. Settings of HMRF: 10,000 initial centroids were used and the best centroid setting was selected to initiate HMRF. Beta (60.0) selected in comparison with randomly shuffled case, and 500 spatially coherent genes. HMRF clustering was repeated for two more times with similar results. (c) Expression patterns of representative marker genes. (d) The anatomical structure identified by hematoxylin and eosin staining.

**Supplementary Fig 19:** Spatial organization of the mouse dentate gyrus as revealed by the HMRF model. This is a 249-gene seqFISH data set (n=696 cells) (Shah *et al* 2016) with single-cell spatial and transcriptomic information. (a) Spatial domains identified by the 5-state HMRF model. Settings of HMRF: 10,000 initial centroids were used and the best centroid was selected to initiate HMRF. Beta (28.0) selected in comparison with randomly shuffled case, and 91 spatially coherent genes. HMRF clustering was repeated two more times with similar results. (b) Schematic of the anatomical structure at dentate gyrus. Rectangular boxes indicate the imaging fields shown in (a). (c) The expression pattern of a number of representative marker genes.

Methods:

**Supplementary Fig 20:** Estimates of imaging bias in the seqFISH data. Cortex (n=1597 cells) is divided into 20 adjacent fields of view (shortened as fields). We divide each field into a 50 bin-by-50 bin grid. Then for each bin, we compute the average expression level at that bin over all 20 fields. Together this forms an overall bias map. Principal component analysis was applied to the bias map to model the most significant bias patterns among genes. The top PCs are shown below representing the major bias patterns.

**Supplementary Fig 21:** Dependency of cell-type mapping accuracy on the number of genes used. (a) Relationship between the 8 major, 22 finer, and 49 minor cell types determined by Tasic et al. (b,c,d) Cross-validation estimated mapping accuracy associated with (b) 8 major, (c) 22 finer, and (d) 49 minor classes.

**Supplementary Fig 22:** Cross-validation estimated mapping accuracy for individual cell types. (a) Receiver operating curves (ROC) for each of the eight major cell types. (b) Cross validation accuracies of individual cell types: astrocytes (n=97), endothelial (n=11), GABA-ergic neurons (n=556), glutamatergic neurons (n=859), microglia (n=22), OPC (n=8), oligodendrocyte.1 (n=21), oligodendrocyte.2 (n=23).

**Supplementary Fig 23:** Robustness analysis of our HMRF model. Agreement between domain assignment using different numbers of top spatially coherent genes. Agreement is quantified by (a) contingency table and (b) adjusted mutual information (left) and the proportion of cells clustered consistently (i.e. the diagonal of matrix in (a)) (right).

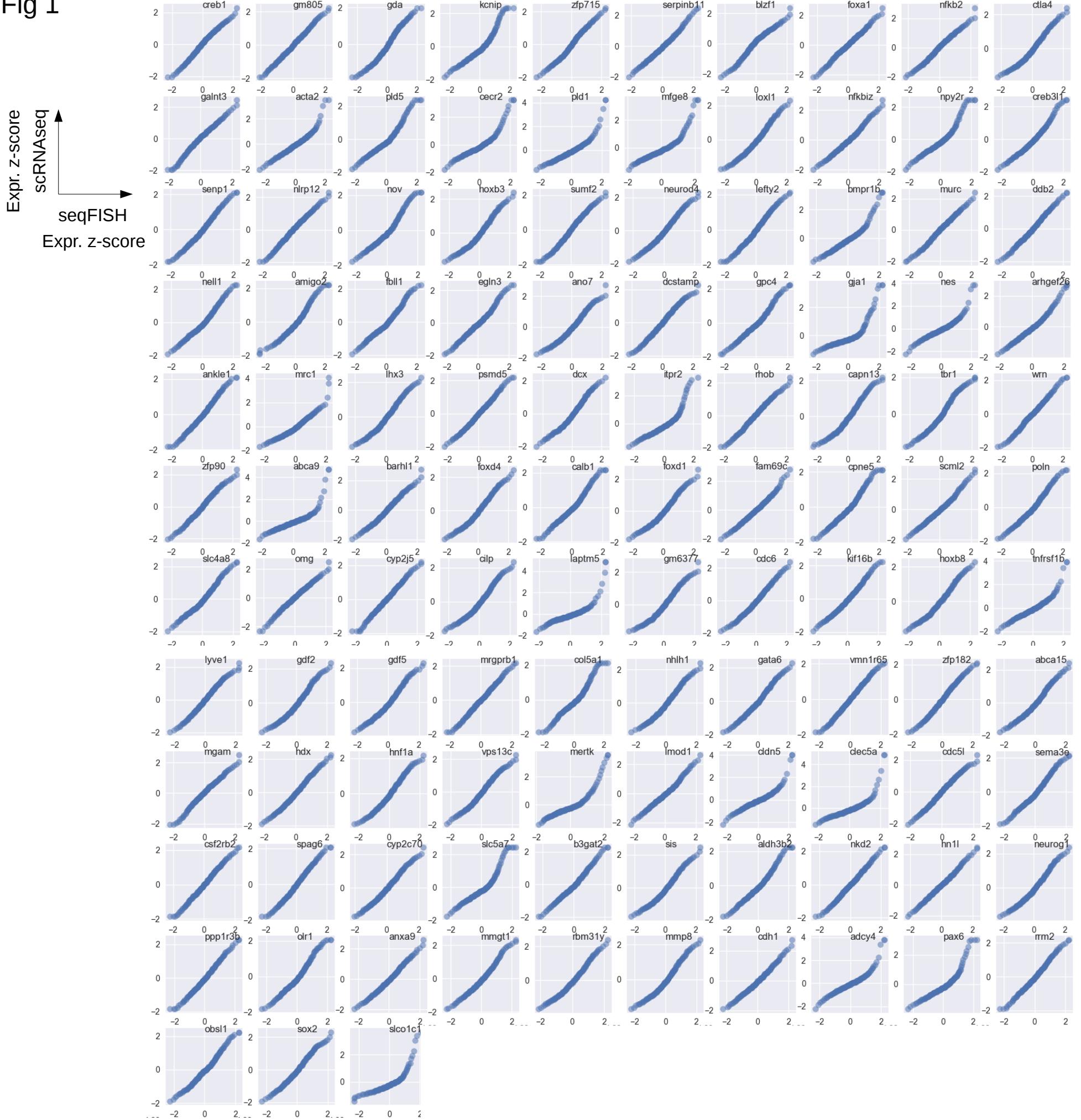
**Supplementary Fig 24:** Robustness analysis of beta in our HMRF model. Agreement between domain assignment using different betas. Agreement is quantified in (a) by the adjusted mutual information (left) and the proportion of cells clustered consistently (right) (i.e. the diagonal of matrix in (b)). (b) Overlap matrix in each case. (c) Spatial pattern comparison. For each beta, 10,000 initial centroid configurations were used to select the best one to initiate HMRF, and HMRF clustering was repeated two more times with similar results.

**Supplementary Fig 25:** Robustness analysis of the HMRF model (n=1597 cells) against disruption of spatial patterns. A subset of cells at various fractions ( $p=0.1, 0.2, 0.4$ , and  $0.99$ ) were randomly selected and switched spatial locations. 100 different random samples were selected for each parameter setting, and the distribution was plotted. For each perturbed dataset, the HMRF model was applied to identify spatial domains. Goodness-of-fit was quantified by using the log-likelihood. Blue vertical line indicates the log-likelihood for the original data set, and is significant compared to shuffling rates of 0.99 (one sided, empirical  $P<0.01$ ), 0.4 ( $P<0.01$ ), and 0.2 ( $P<0.03$ ).

**Supplementary Fig 26:** SeqFISH expression z-scores (n=199,625 values) approximately follow a normal distribution.

**Supplementary Fig 27:** Domain signatures obtained by non-parametric Mann-Whitney U test. (a) general domain signature, complementary to Fig 2d. Cell numbers contained in each domain: O2 (n=109), I1a (n=389), O4 (n=120), I1b (n=79), O1 (n=135), I2 (n=117), I3 (n=205), O3 (n=270), and IS (n=173); (b) glutamatergic restricted signature, complementary to Fig 3b, middle panel. Cell numbers in each domain: O2 (n=79), I1a (n=187), O4 (n=88), I1b (n=58), O1 (n=93), I2 (n=60), I3 (n=73), O3 (n=129), and IS (n=92).

SFig 1



## SFIG 2

**a****Baseline:**

69-gene HMRF (already removed 11 cell type (ct) genes)

**Minus.5.ct.genes:**

remove 5 additional ct genes (64-gene HMRF)

**Minus.3.ct.genes:**

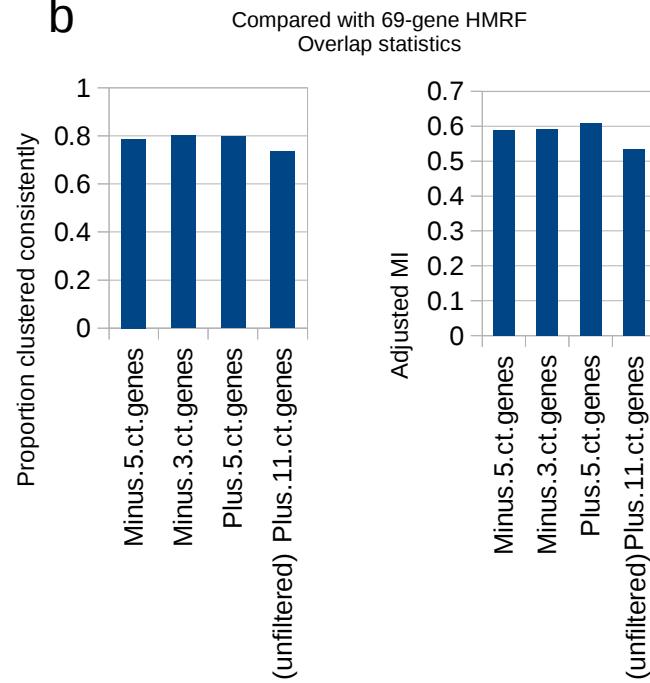
remove 3 additional ct genes (66-gene HMRF)

**Plus.5.ct.genes:**

add back 5 ct genes (74-gene HMRF)

**Plus.11.ct.genes (unfiltered):**

add back all 11 ct genes (80-gene HMRF)

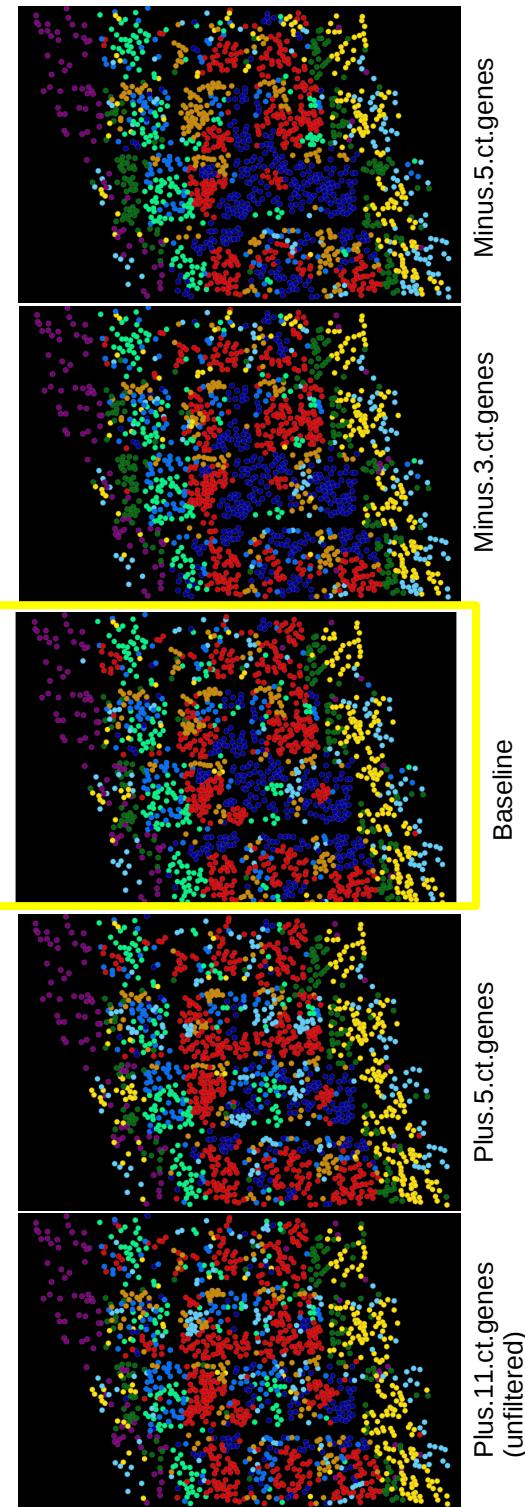
**b****c**Compared with 69-gene HMRF  
Overlap matrices

Minus.5.ct.genes HMRF										
277	5	3	0	0	0	20	0	0	20	
8	83	1	0	0	0	9	0	0	7	
8	3	74	0	26	0	0	0	0	4	
5	0	8	113	23	9	0	0	1	0	
13	1	13	3	130	6	0	0	0	0	
0	0	3	1	5	67	0	0	0	0	
23	7	0	0	0	0	124	1	2		
23	6	6	4	2	0	0	119	12		
41	6	12	0	1	0	12	14	233		

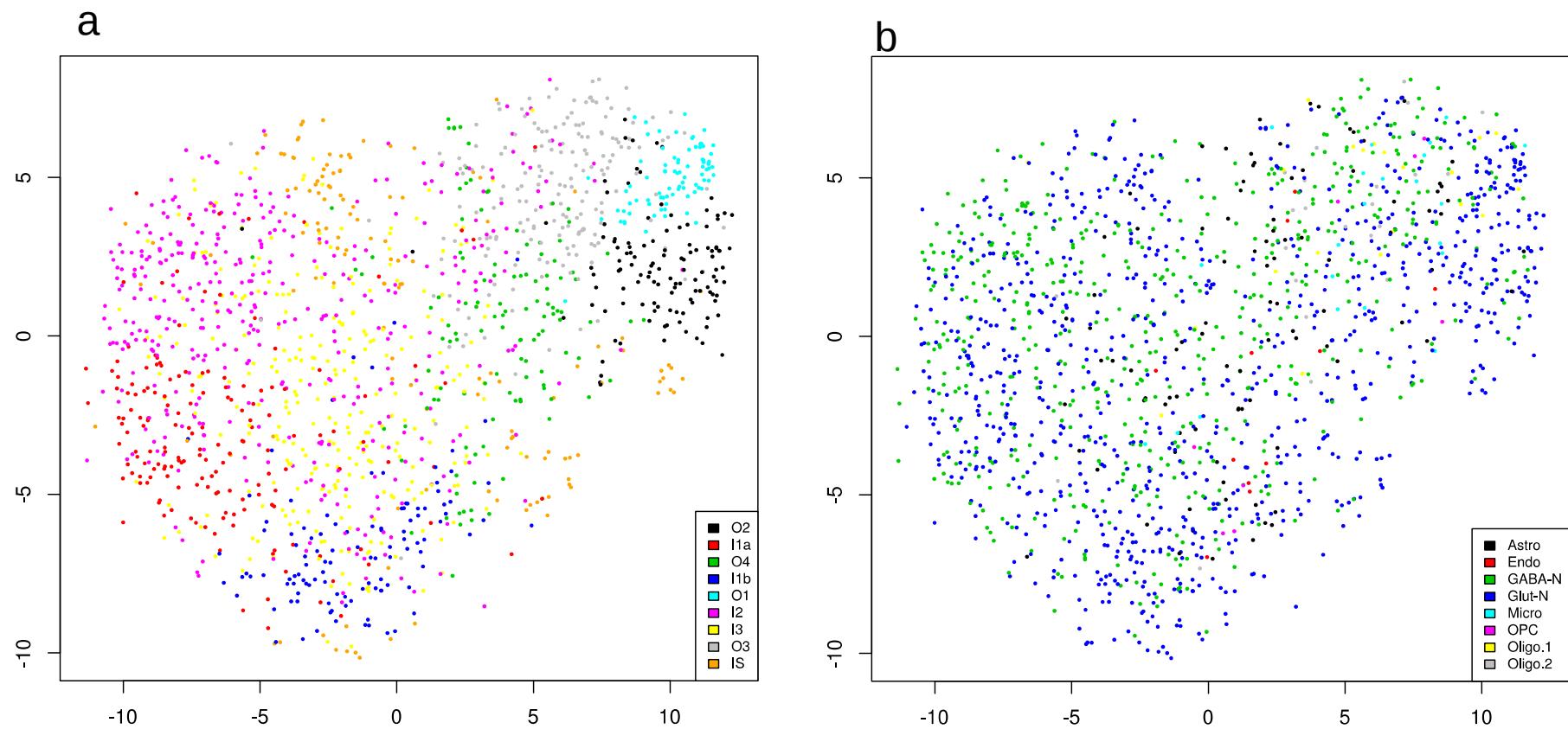
Minus.3.ct.genes HMRF										
81	5	11	2	17	0	0	0	2	3	
3	233	45	7	1	1	0	15	5		
2	23	29	15	3	0	1	23	8		
8	8	6	104	1	0	0	0	0	2	
15	1	11	2	142	4	3	2	1		
2	0	1	0	5	72	2	0	0		
9	0	6	1	18	5	115	0	0		
0	1	17	3	0	0	0	114	3		
0	7	10	1	0	0	0	9	89		

Plus.5.ct.genes HMRF										
86	28	3	3	0	11	0	1	0		
5	144	5	5	0	4	0	0	0	1	
0	10	99	2	0	2	0	0	0	1	
7	62	17	34	0	10	1	3	2		
0	0	0	73	0	1	5	1	5	1	
3	13	1	3	0	130	1	0	0		
0	1	0	3	7	1	171	12	26		
0	3	1	7	2	0	4	100	3		
10	17	9	28	0	7	9	0	86		

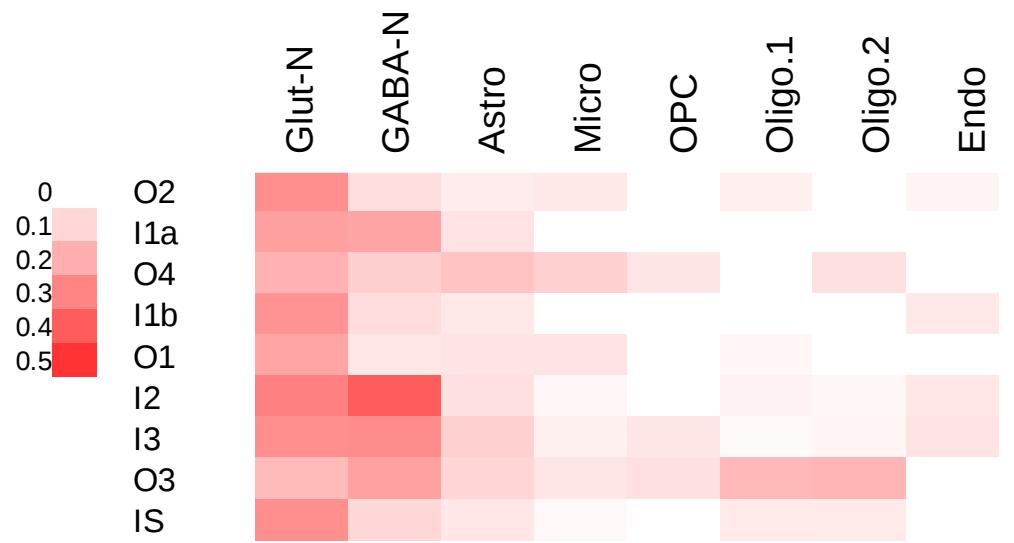
Plus.11.ct.genes HMRF (unfiltered)										
74	5	8	0	0	1	1	0	0	0	
3	99	16	0	1	3	4	0	3		
5	12	154	2	1	38	1	1	1		
0	0	0	113	15	0	5	5	5	1	
0	0	1	5	110	4	14	3	2		
0	2	6	9	25	68	18	7	11		
0	2	2	22	85	2	341	8	17		
0	0	0	12	31	0	7	84	4		
0	1	0	2	10	4	7	3	96		

**d**

SFig 3



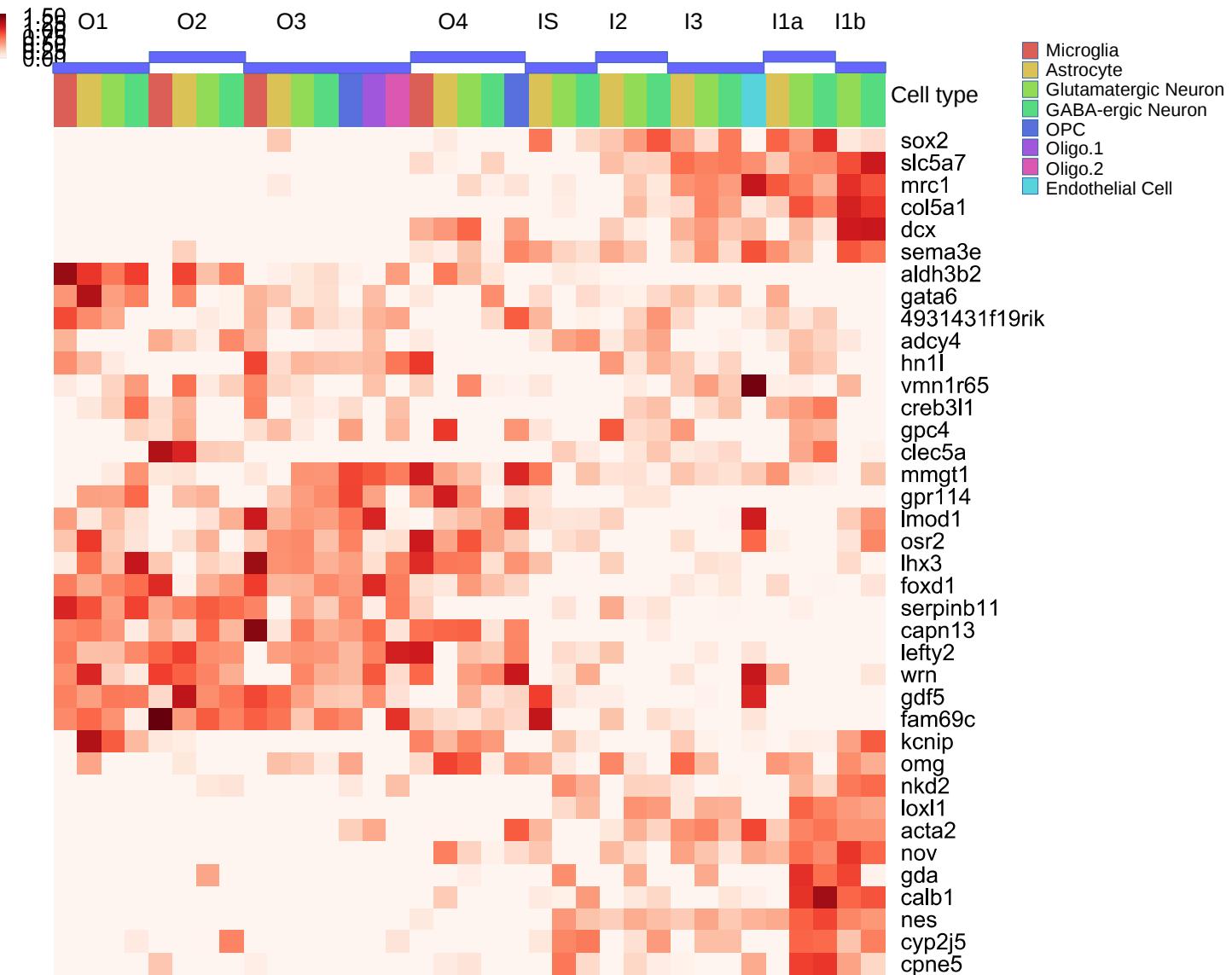
SFig 4



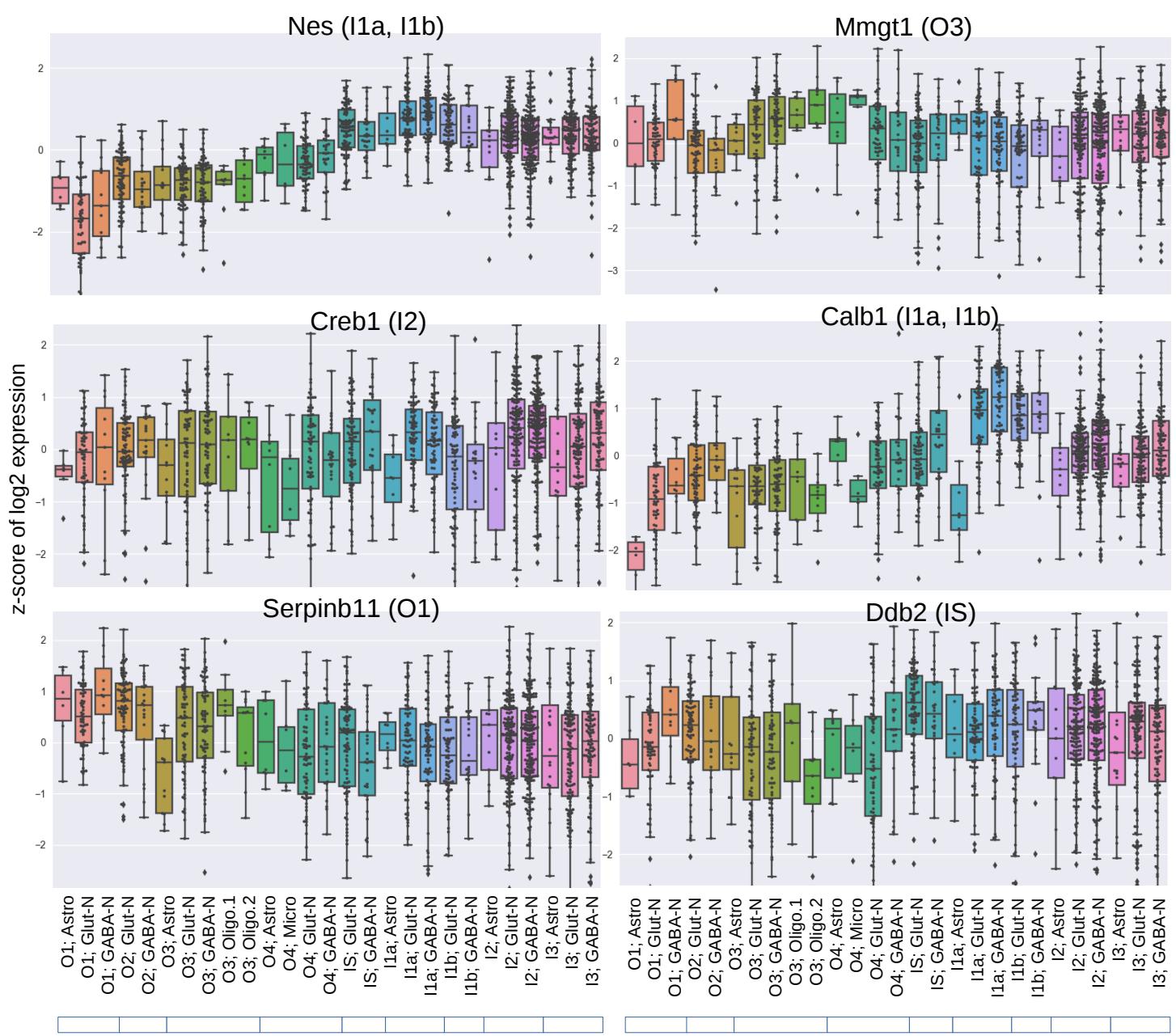
SFig 5



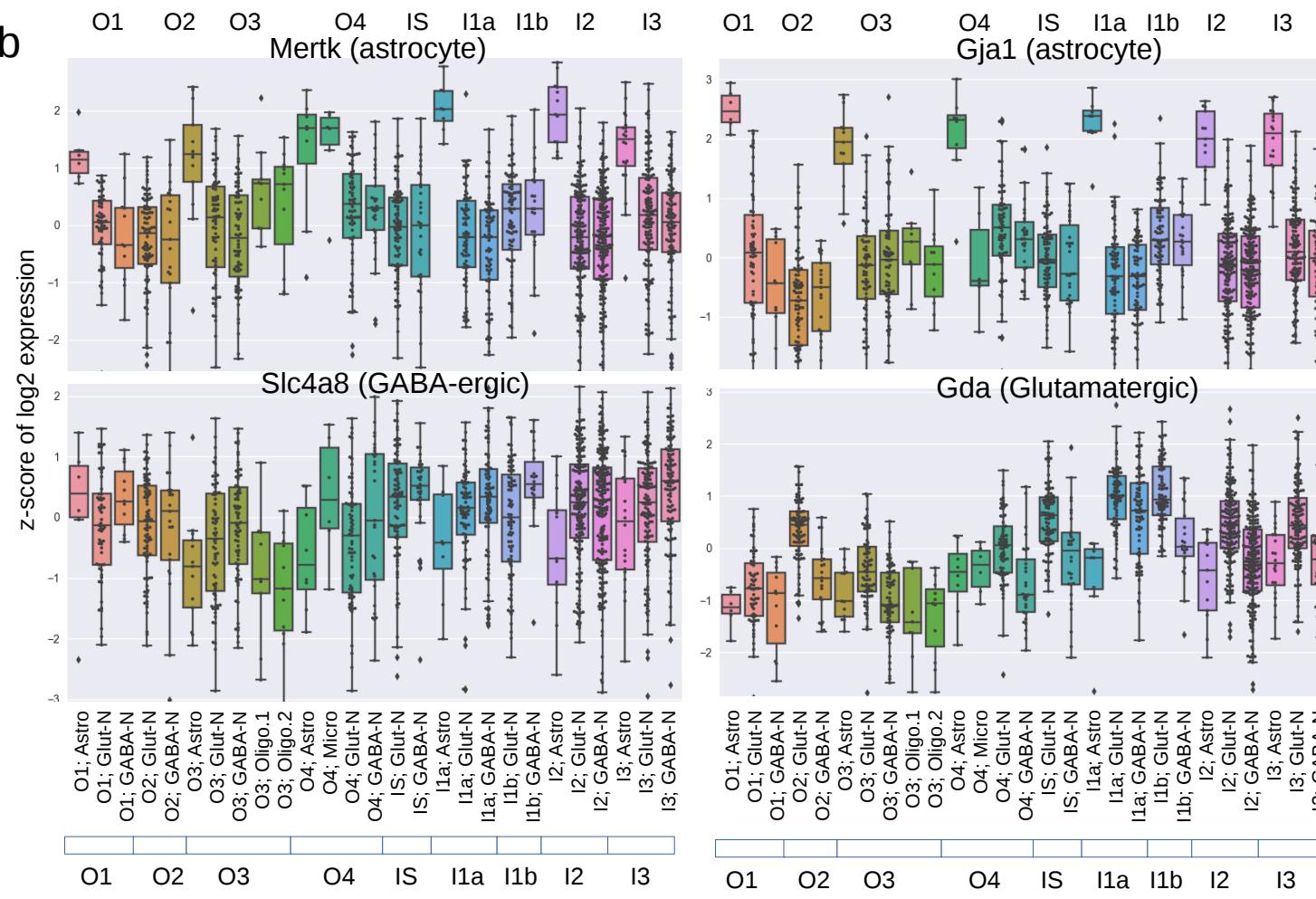
SFig 6

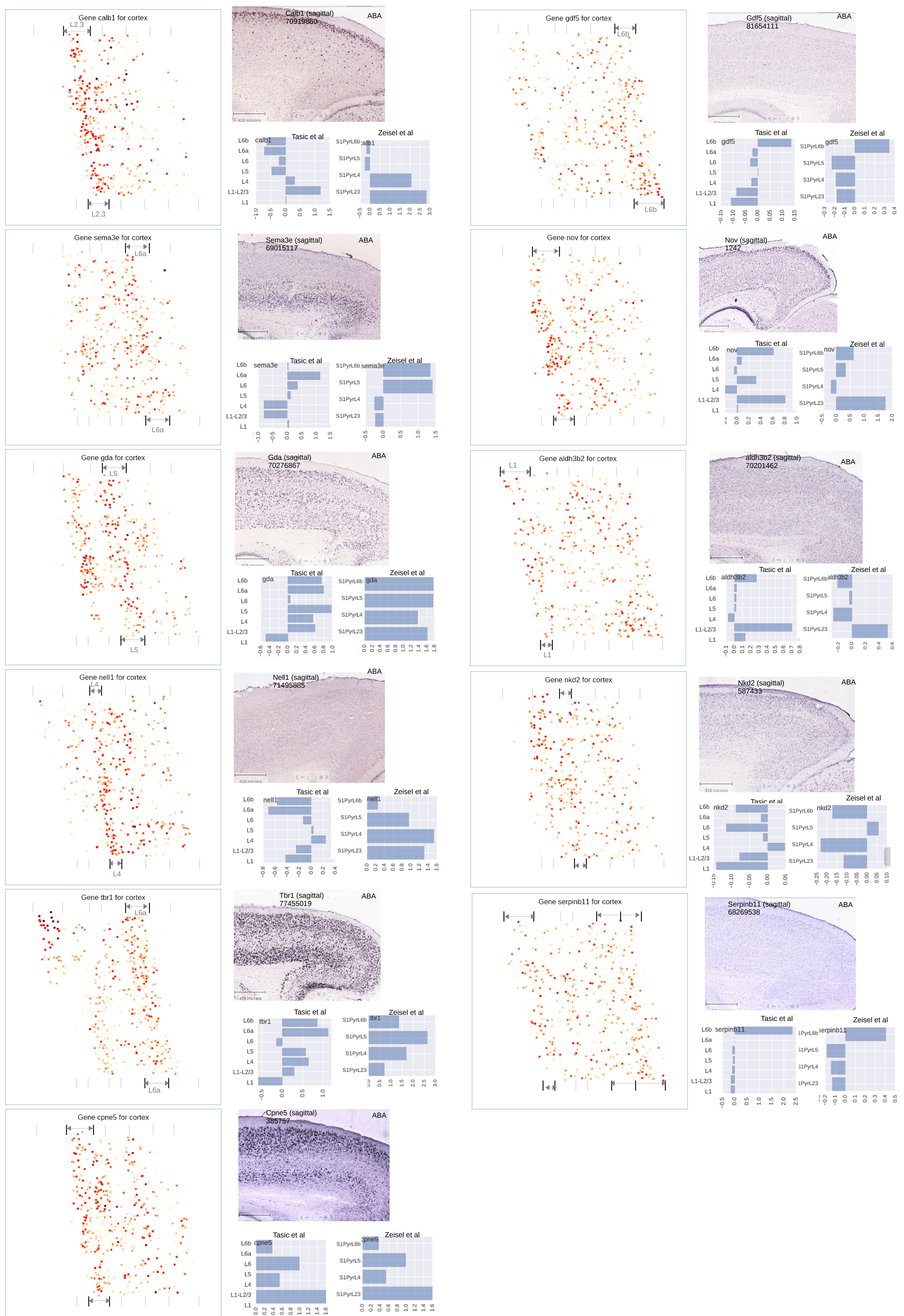


SFig 7 a

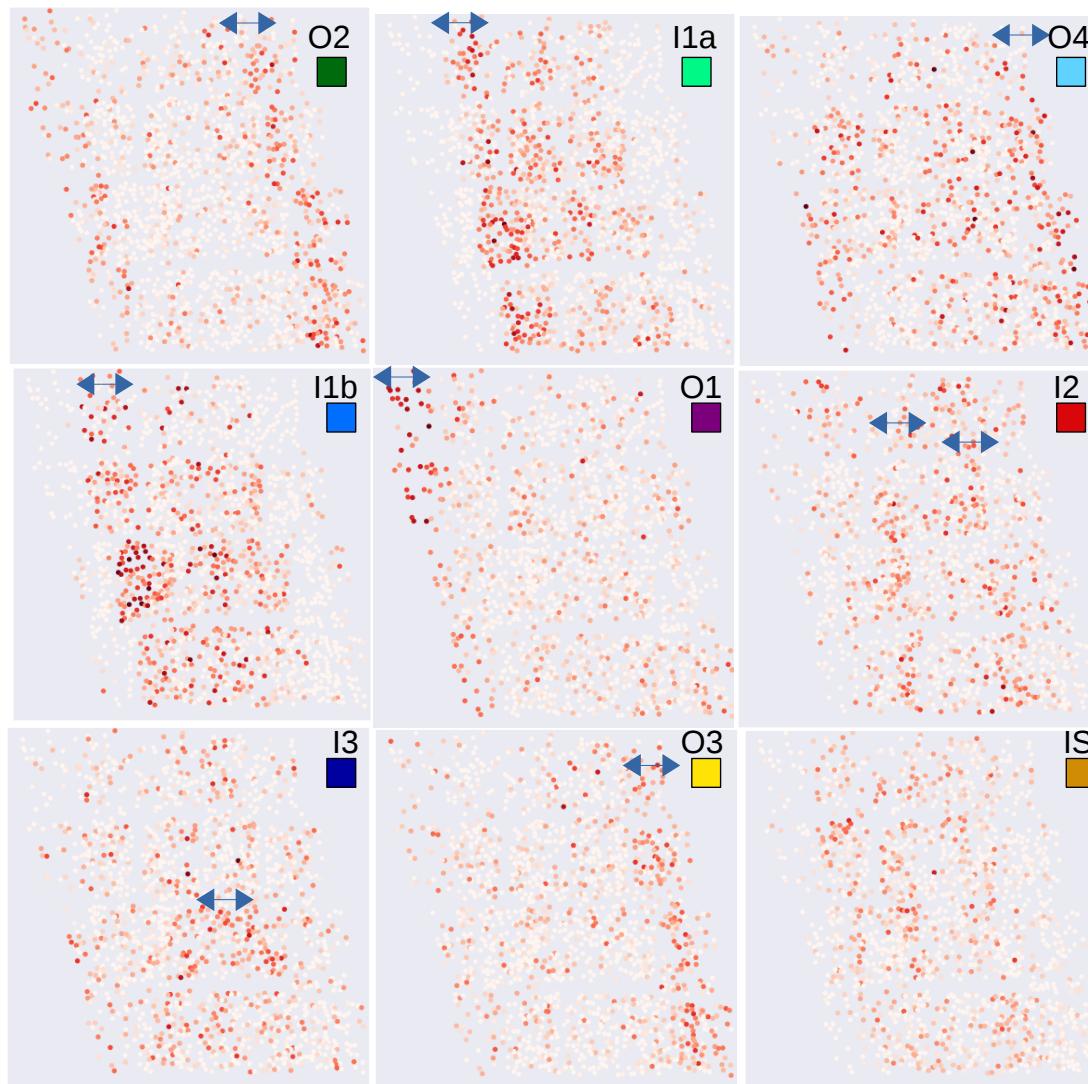
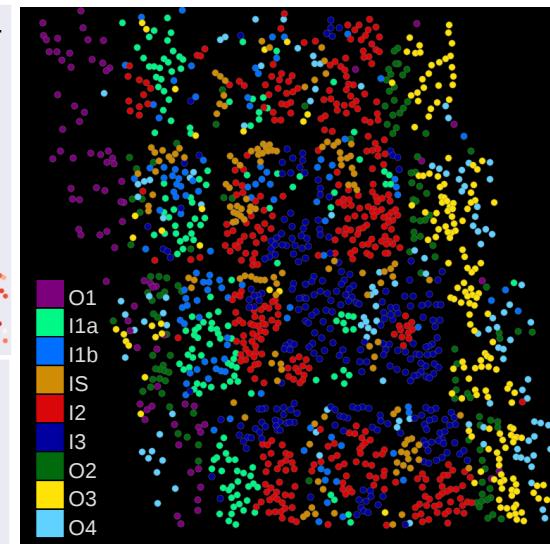


b



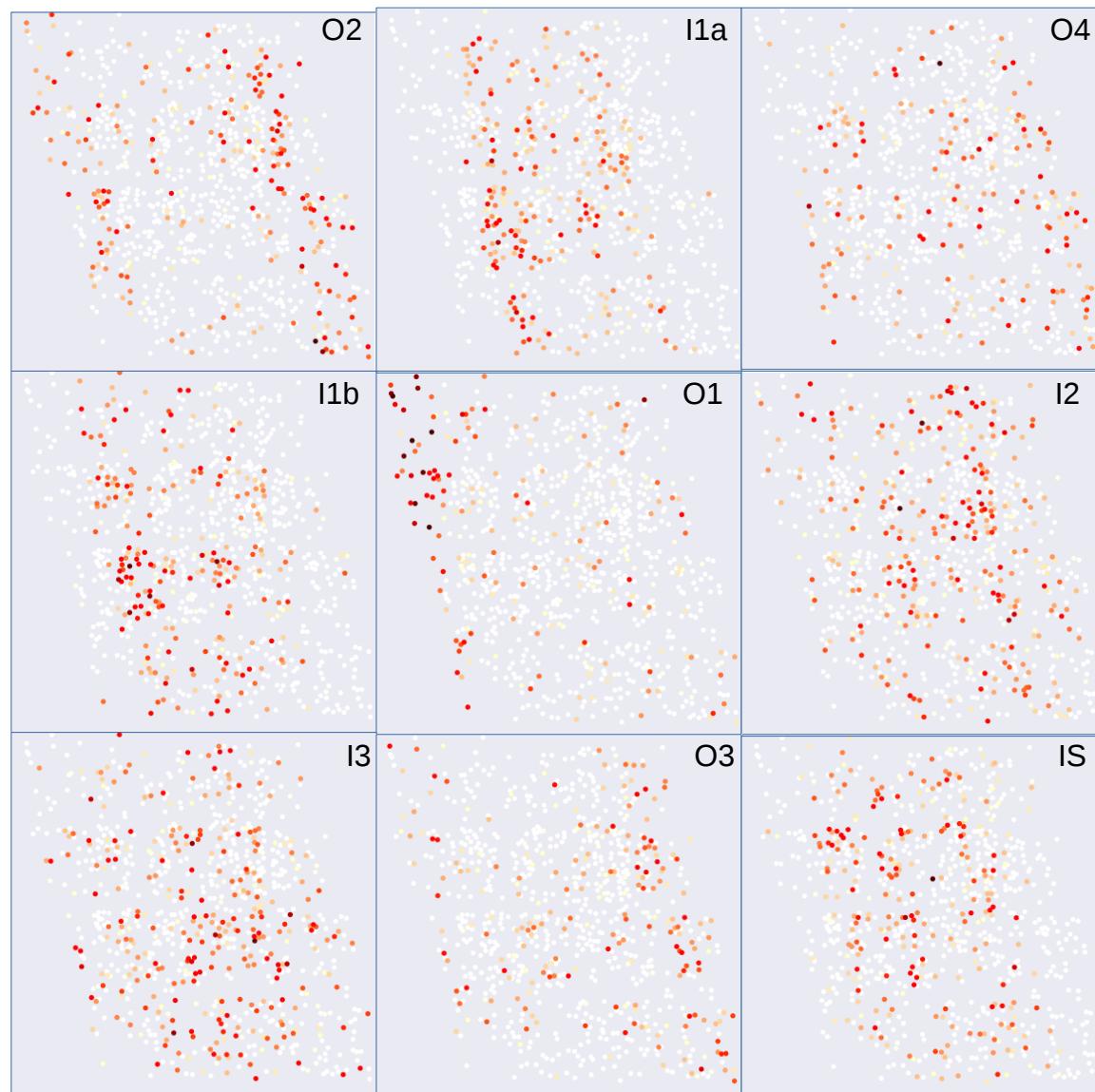


SFig 9

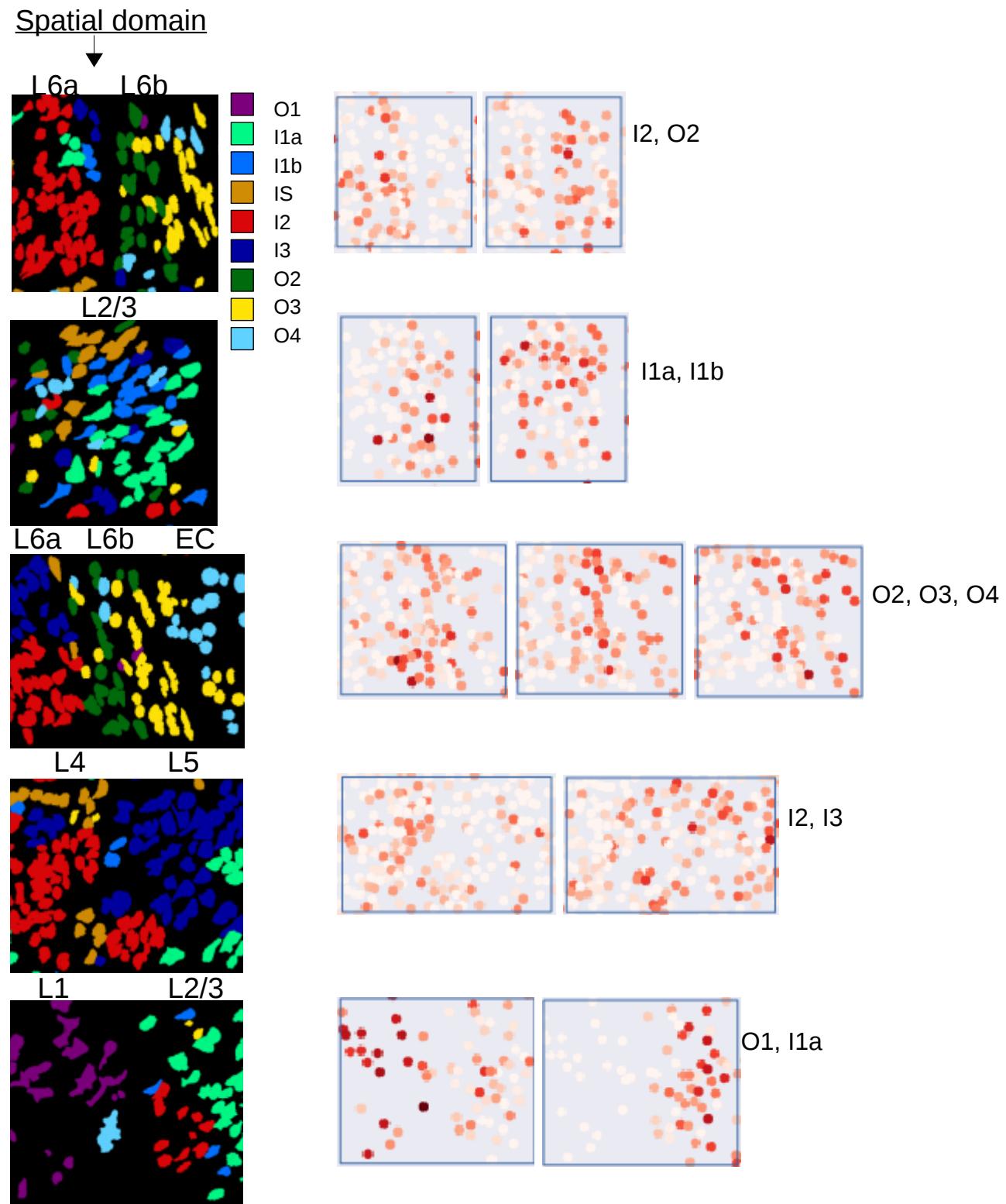
**a****b**

SFig 10

## Glutamatergic cells

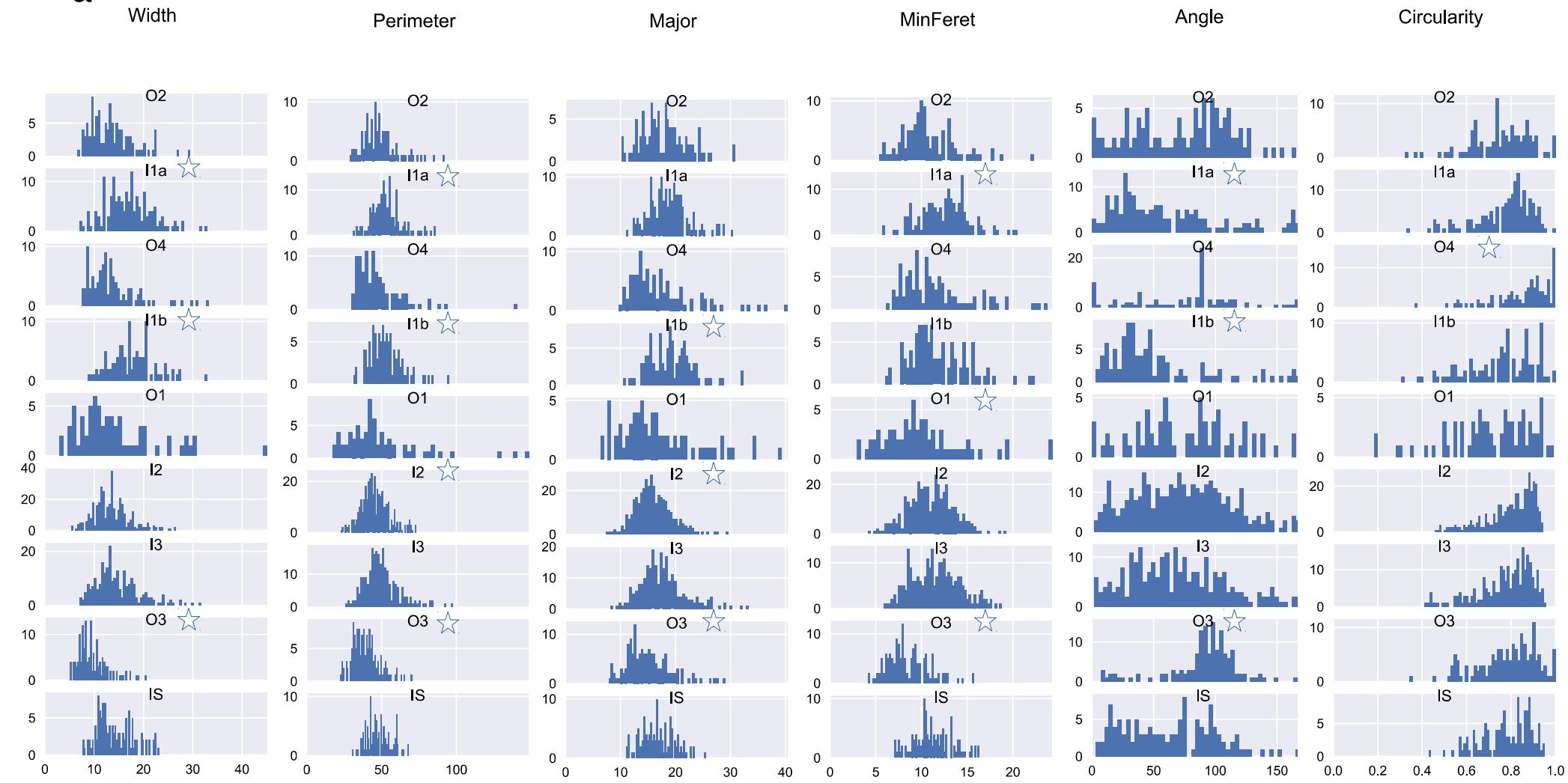


SFig 11



SFig 12

a



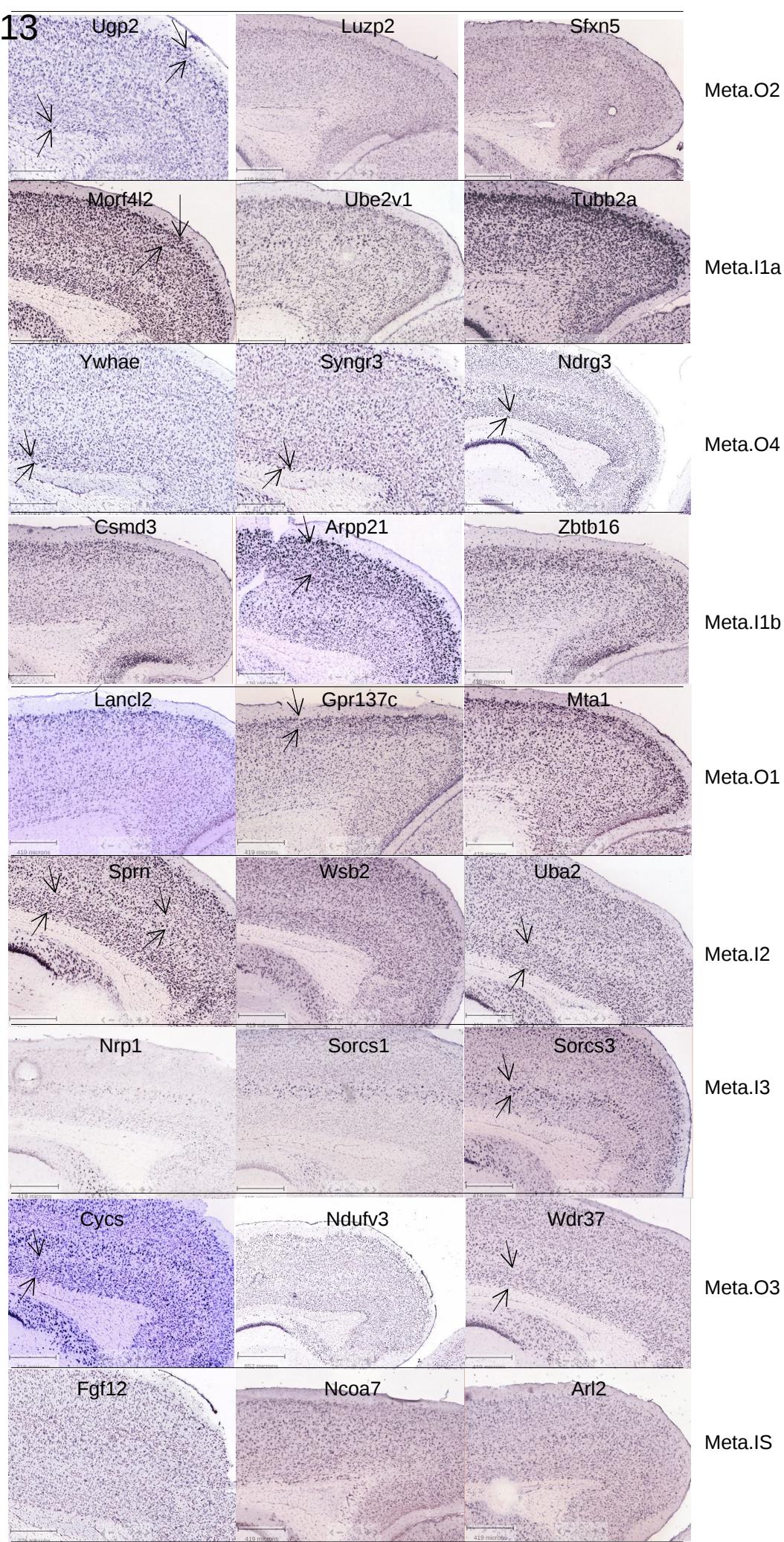
b

## Glutamatergic Cells

	Perimeter	Width	Angle	MinFeret	Circularity	Major
O2	-	-	-	-	-	-
I1a	1.78E-05	3.60E-08	8.17E-06	-	-	-
O4	-	-	-	-	7.00E-12	-
I1b	-	1.75E-10	7.90E-08	-	-	-
O1	-	-	-	0.00288	4.46E-05	-
I2	-	-	-	-	-	3.89E-05
I3	-	0.0158	-	-	-	-
O3	4.46E-10	1.26E-19	2.53E-10	8.67E-14	-	-
IS	-	-	-	-	-	-

## All cells

	Perimeter	Width	Angle	MinFeret	Circularity	Major
O2	-	-	-	-	-	-
I1a	1.07E-14	4.34E-17	-	3.02E-11	-	-
O4	-	-	-	-	6.18E-12	-
I1b	1.24E-05	1.60E-14	6.28E-11	-	-	2.74E-06
O1	-	-	-	0.002773	-	-
I2	-	-	-	-	-	1.30E-08
I3	-	-	-	-	-	-
O3	2.32E-20	6.80E-37	6.70E-18	5.27E-26	-	1.50E-10
IS	-	-	-	-	-	-

**SFig 13**

SFig 14

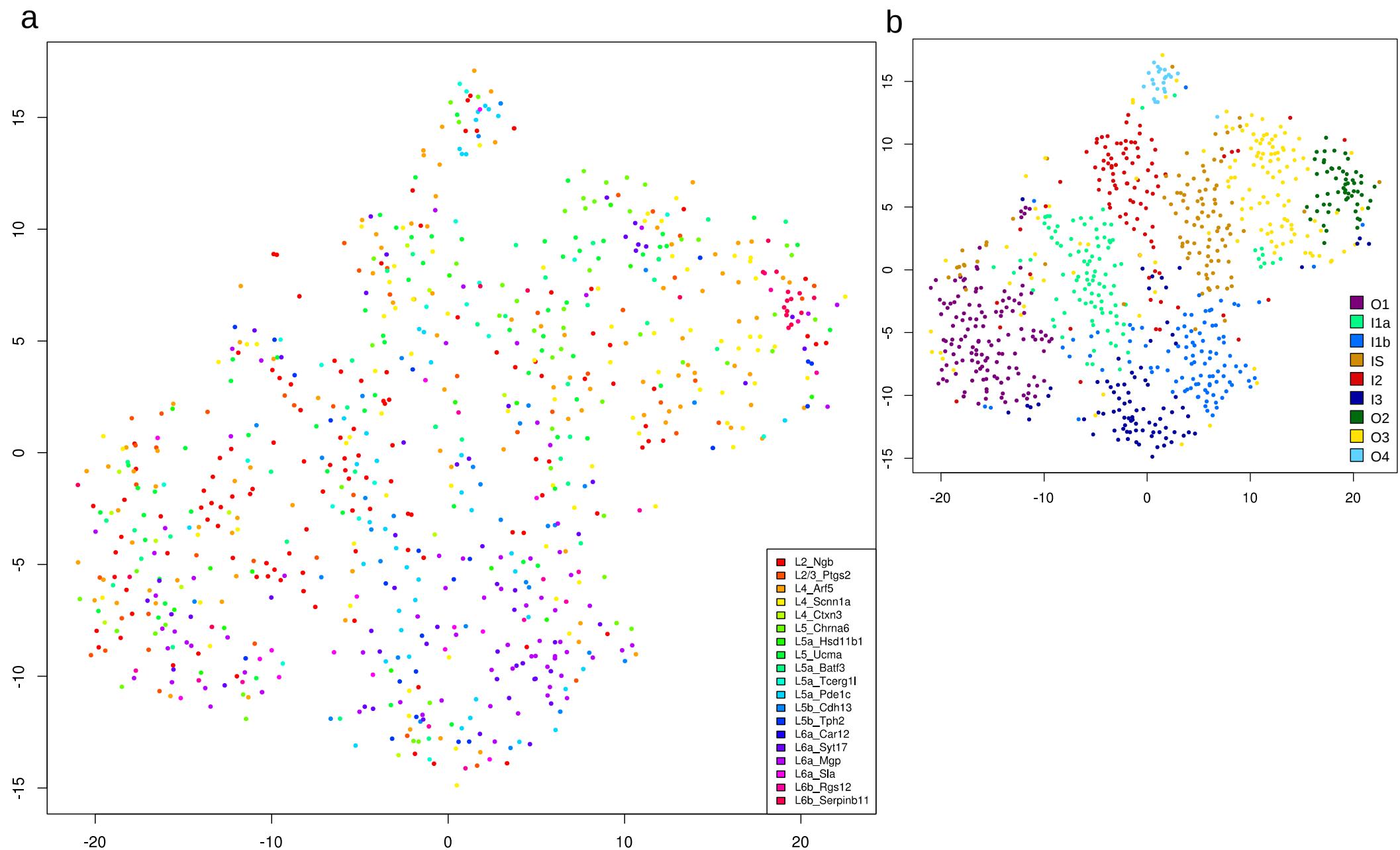
## Gene overlap (within 125 genes)

$-\log_{10}(P)$		I1a	I1b	I2	I3	IS	O1	O2	O3	O4
0	L2/3_Ptgs2	10.2	2.3	0.5	1.1	3.7	5.7	2.5	0.8	3.7
2	L2_Ngb	9.4	2.8	0.7	1.4	2.7	2.8	1.3	1.0	4.2
4	L4_Arf5	3.9	2.3	1.2	2.7	2.2	3.9	2.5	1.9	1.5
6	L4_Ctxn3	1.9	0.8	10.0	1.0	0.7	0.8	3.8	7.4	1.4
8	L4_Scnn1a	1.5	1.5	10.0	0.8	0.5	4.0	1.7	7.5	1.1
10	L5_Chrna6	1.5	1.5	1.0	1.7	1.5	6.2	3.9	3.2	2.1
	L5_Ucma	1.4	5.6	2.2	6.3	1.4	1.4	1.5	1.2	2.0
	L5a_Batf3	2.8	2.8	2.9	1.4	2.7	2.8	1.3	1.0	1.8
	L5a_Hsd11b1	1.3	3.1	2.0	1.5	5.0	1.3	1.4	2.7	1.9
	L5a_Pde1c	1.5	3.6	2.5	4.0	1.5	1.5	1.7	1.4	2.1
	L5a_Tcerg1l	1.0	2.0	1.5	2.2	2.0	2.0	2.1	1.8	2.6
	L5b_Cdh13	4.5	6.6	1.5	5.2	4.3	1.1	1.2	0.9	1.0
	L5b_Tph2	6.1	10.8	0.5	4.9	2.3	1.0	1.1	2.1	3.9
	L6a_Car12	3.6	3.6	1.0	4.0	1.5	1.5	1.7	1.4	2.1
	L6a_Mgp	0.8	8.9	10.0	4.0	0.7	0.8	2.2	2.7	1.4
	L6a_Sla	1.1	9.0	1.5	3.1	1.1	2.6	2.9	2.3	1.7
	L6a_Syt17	5.6	5.6	0.9	6.3	1.4	1.4	1.5	1.2	2.0
	L6b_Rgs12	1.7	1.0	1.2	4.5	1.7	1.7	1.8	1.5	2.3
	L6b_Serpinb11	1.3	1.3	2.0	1.5	3.0	3.1	8.4	4.6	1.9

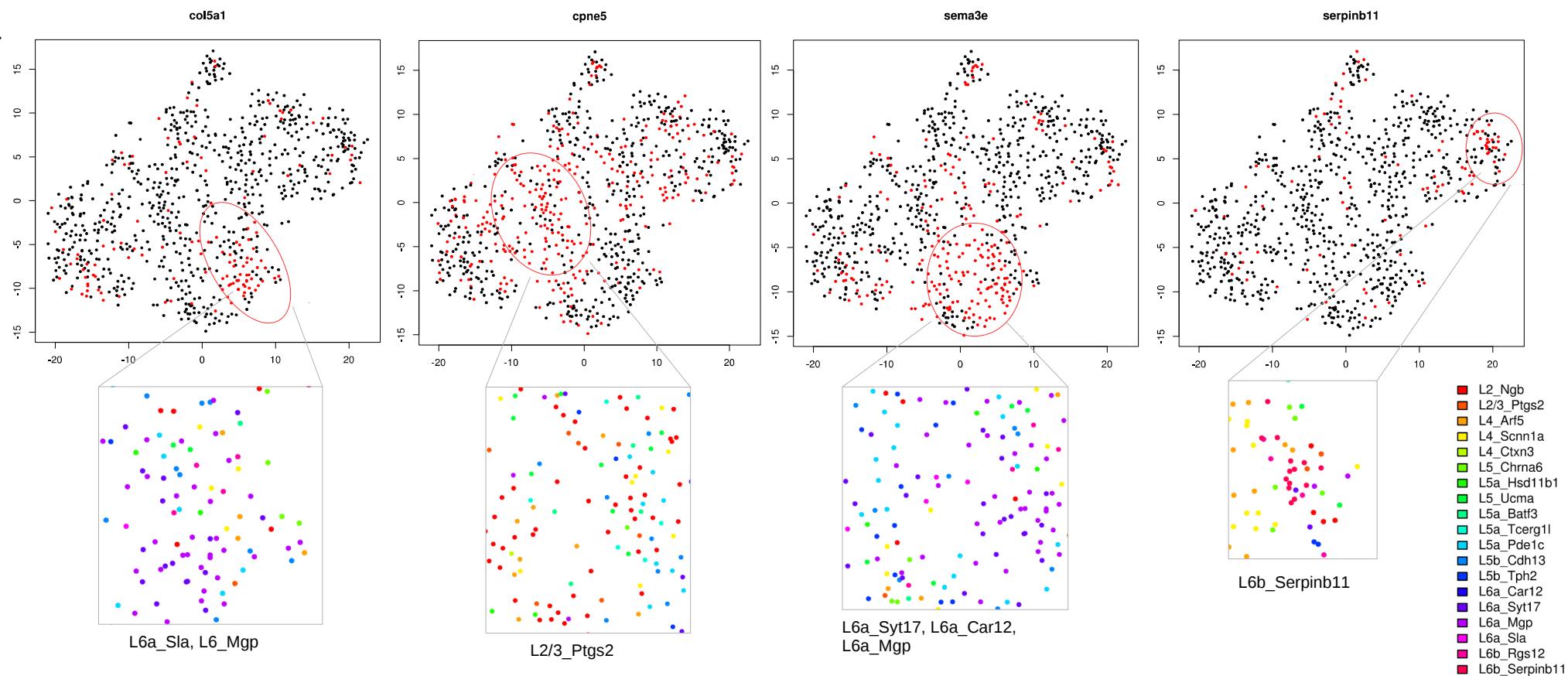
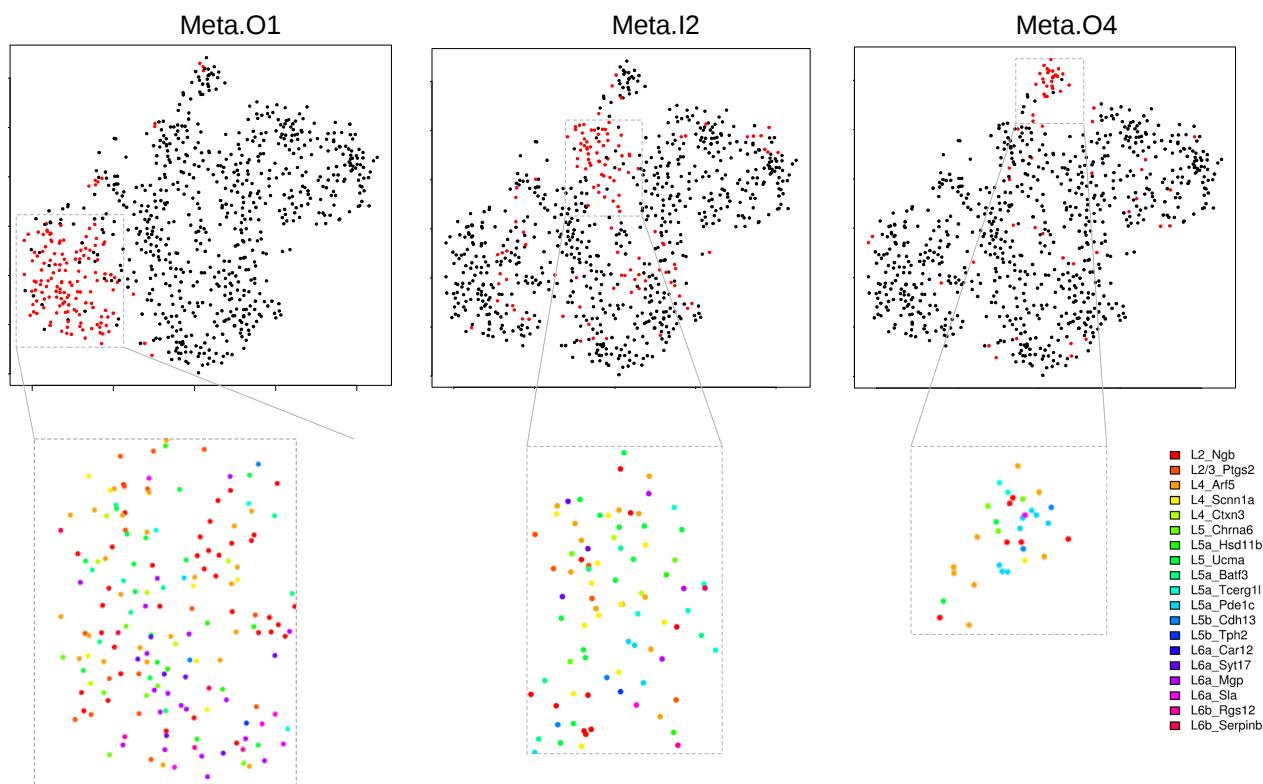
## Cell overlap

	I1a	I1b	I2	I3	IS	O1	O2	O3	O4
L2/3_Ptgs2	10.1	0.0	0.0	0.0	0.8	3.3	0.0	0.0	0.1
L2_Ngb	1.5	1.0	0.1	0.0	0.1	1.0	0.1	0.2	2.7
L4_Arf5	0.2	0.0	0.9	0.1	0.6	1.8	0.2	1.1	0.1
L4_Ctxn3	0.2	0.1	0.8	0.1	0.3	0.0	2.8	2.1	0.0
L4_Scnn1a	0.0	0.0	0.9	0.0	0.3	0.4	0.9	4.4	0.1
L5_Chrna6	0.1	0.1	0.4	0.5	0.4	3.3	0.3	0.6	0.6
L5_Ucma	0.1	0.2	0.6	1.1	0.5	1.5	0.2	0.6	0.4
L5a_Batf3	0.4	0.0	3.8	0.0	2.1	0.3	0.1	0.2	0.6
L5a_Hsd11b1	0.0	0.0	0.1	0.3	2.7	0.0	0.8	2.7	1.3
L5a_Pde1c	1.2	0.0	1.8	0.5	0.4	0.1	0.1	0.4	1.9
L5a_Tcerg1l	0.2	0.0	0.4	0.1	3.5	0.5	0.0	1.4	0.2
L5b_Cdh13	2.1	0.9	0.5	1.6	0.0	0.0	0.0	0.1	5.3
L5b_Tph2	0.7	3.1	0.1	1.0	0.3	0.0	0.0	0.2	1.3
L6a_Car12	0.6	0.1	0.6	6.7	0.0	0.0	0.7	0.0	0.3
L6a_Mgp	0.1	2.5	0.2	3.3	0.0	0.2	0.1	0.1	0.1
L6a_Sla	0.0	12.9	0.0	0.9	0.0	1.4	0.0	0.0	0.1
L6a_Syt17	0.3	1.6	0.6	1.2	0.3	0.3	0.2	0.1	1.2
L6b_Rgs12	0.1	3.0	0.3	0.7	0.1	0.7	1.8	0.0	0.5
L6b_Serpinb11	0.0	0.0	0.1	0.4	0.4	14.2	0.1	0.4	

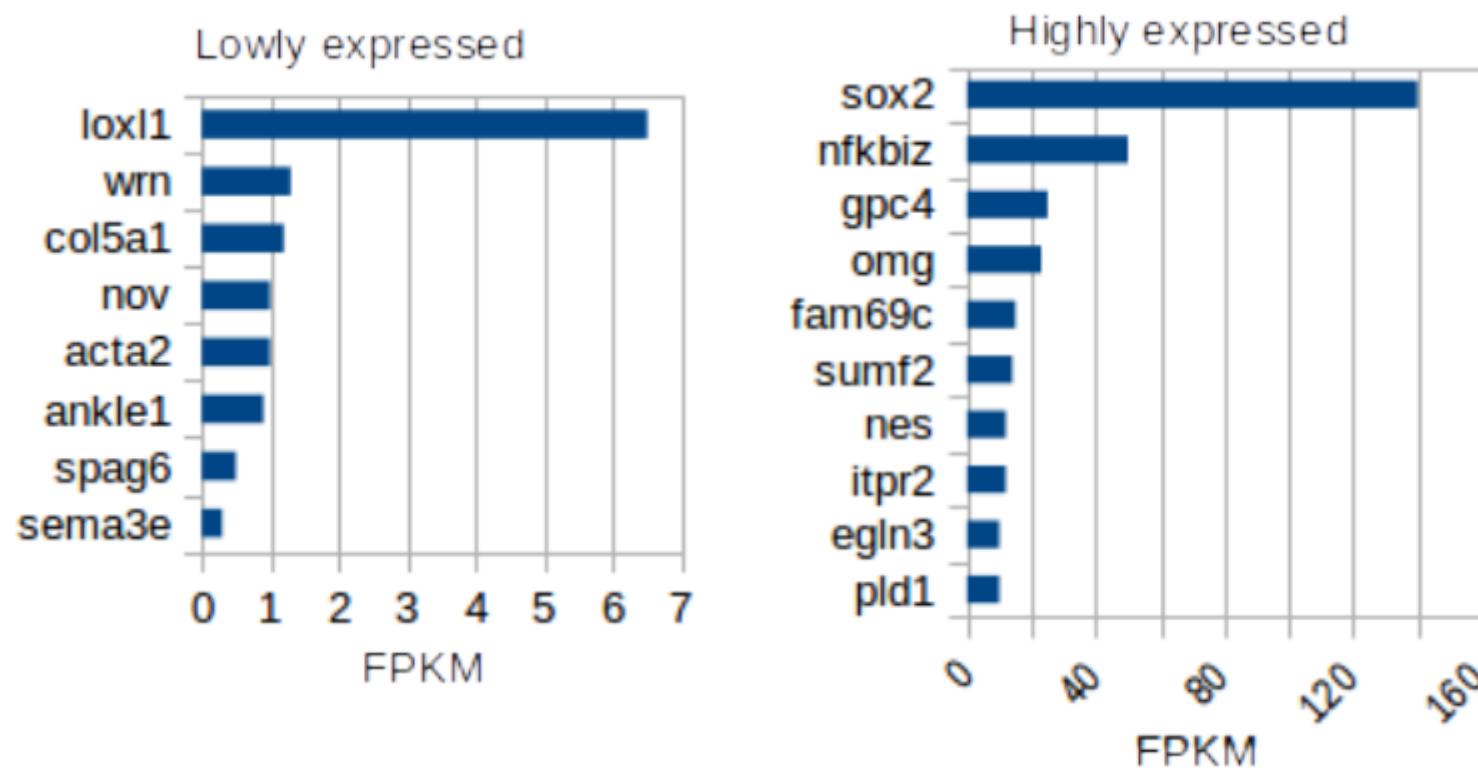
SFig 15



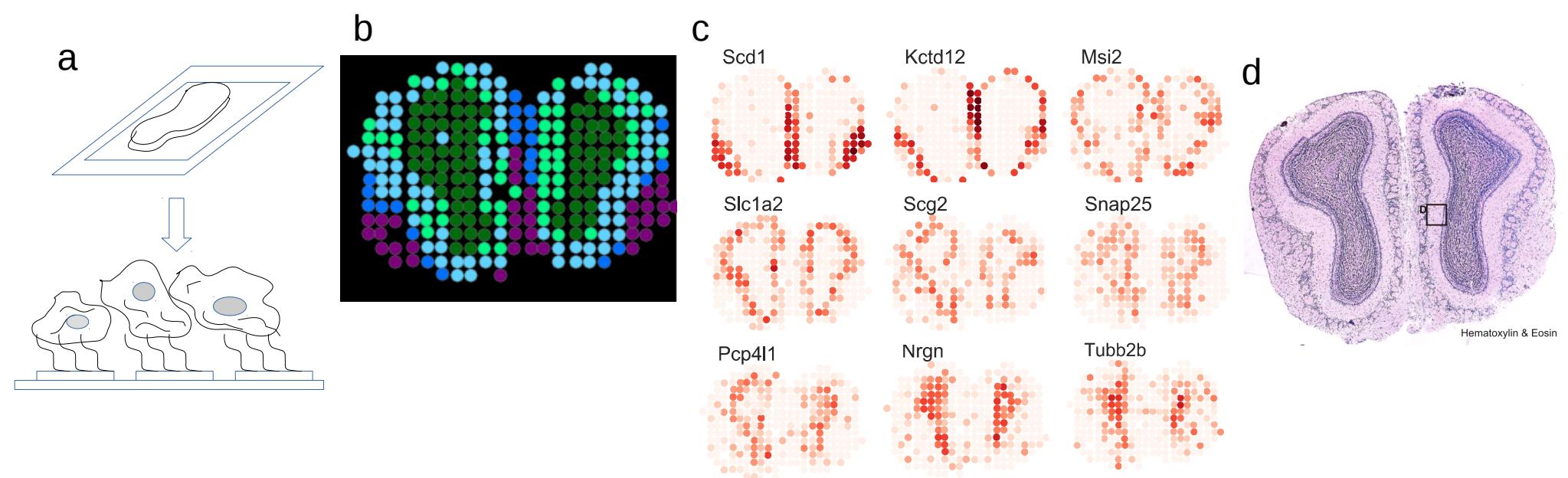
SFig 16

**a****b**

SFig 17

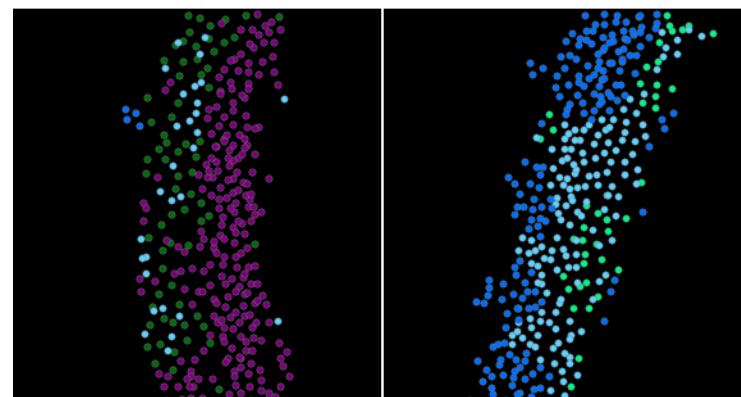


SFig 18

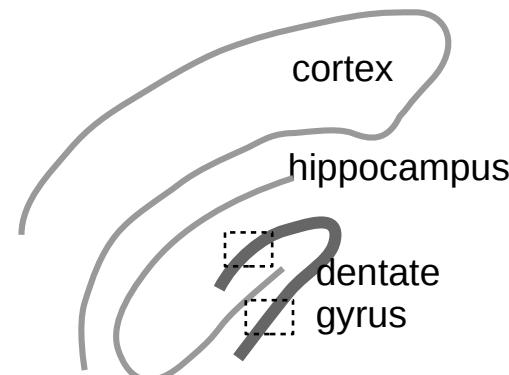


SFig 19

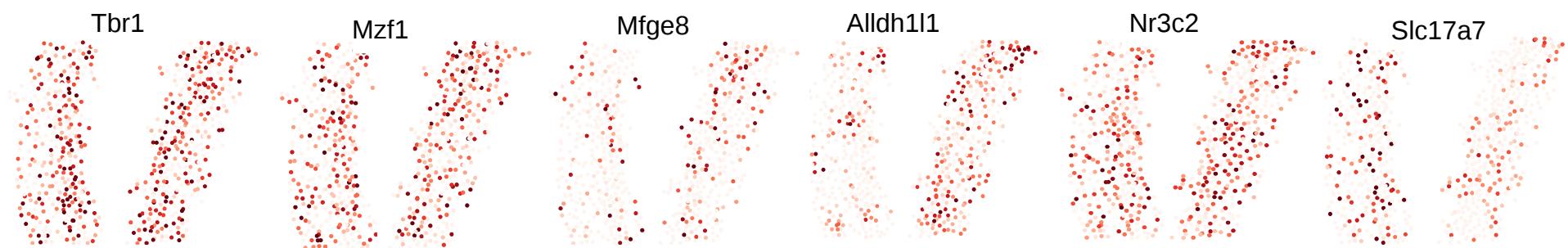
a



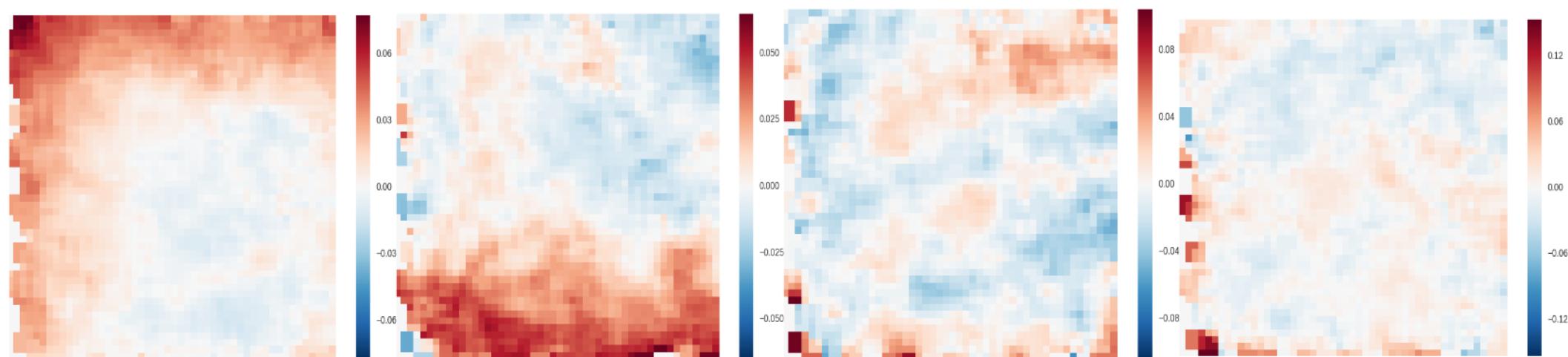
b



c



SFig 20



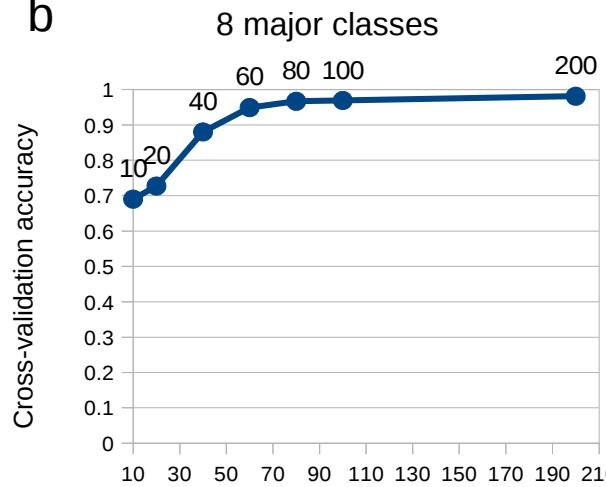
## SFig 21

a

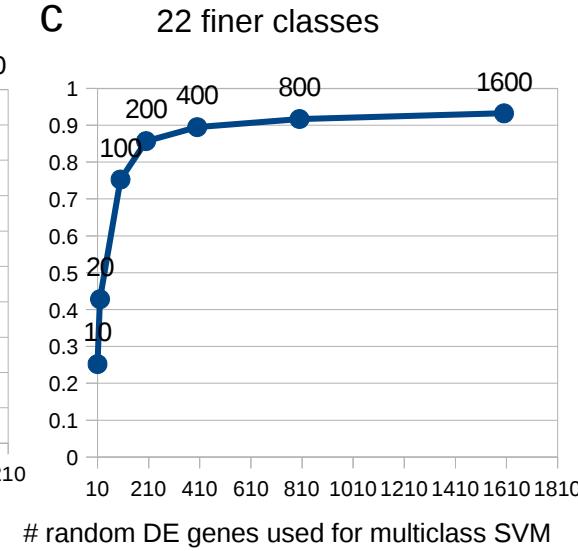
8 major classes  
22 finer classes  
49 minor classes

Oligo_96_Rik	Oligo.1	Oligo.1
Oligo_Opalin	Oligo.2	Oligo.2
OPC_Pdgfra	OPC	OPC
Astro_Gja1	Astro	Astro
Micro_Ctss	Micro	Micro
Endo_Myl9	Endo	Endo
Endo_Tbc1d4		
L2/3_Ptgss2	L2/3	
L2_Ngb		
L6a_Car12	L6a	
L6a_Syt17		
L4_Arf5	L4_Arf5	
L4_Ctxn3	L4_Ctxn3/	
L4_Scnn1a	Scnn1a	
L5_Ucma	L5_Ucma /	
L5_Chma6	Chma6	
L5a_Pde1c		
L5a_Hsd11b1	L5a	
L5a_Batf3		
L5a_Tcerg1		
L5b_Cdh13	L5b	
L5b_Tph2		
L6a_Mgp	L6a	
L6a_Sla		
L6b_Rgs12	L6b	
L6b_Serp1b11		
Vip_Mybpcl		
Vip_Parm1	Vip	
Vip_Chat		
Vip_Gpc3		
Sncg	Sncg	
Vip_Sncg		
Ndnf_Car4		
Ndnf_Cxcl14	Ndnf	
Igtp		
Smad3	Igtp/Smad3	
Sst_Chodl		
Sst_Tacstd2		
Sst_Th	Sst	
Sst_Cbln4		
Sst_Cdk6		
Sst_Myh8		
Pvalb_Obox3		
Pvalb_Rspoz2		
Pvalb_Tacr3	Pvalb_1	
Pvalb_Wt1		
Pvalb_Cpn5		
Pvalb_Gpx3	Pvalb_2	
Pvalb_Tpbg		

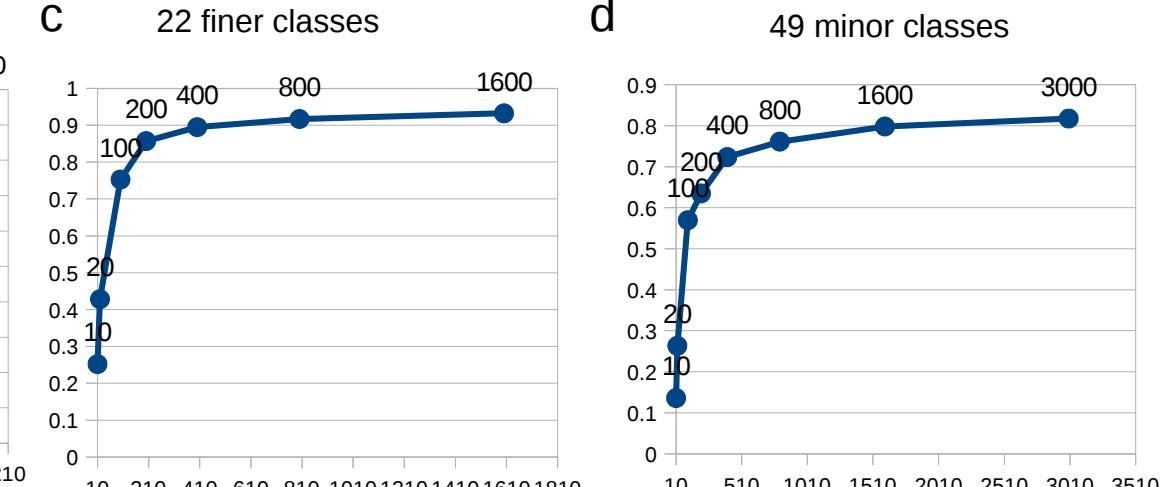
b



c

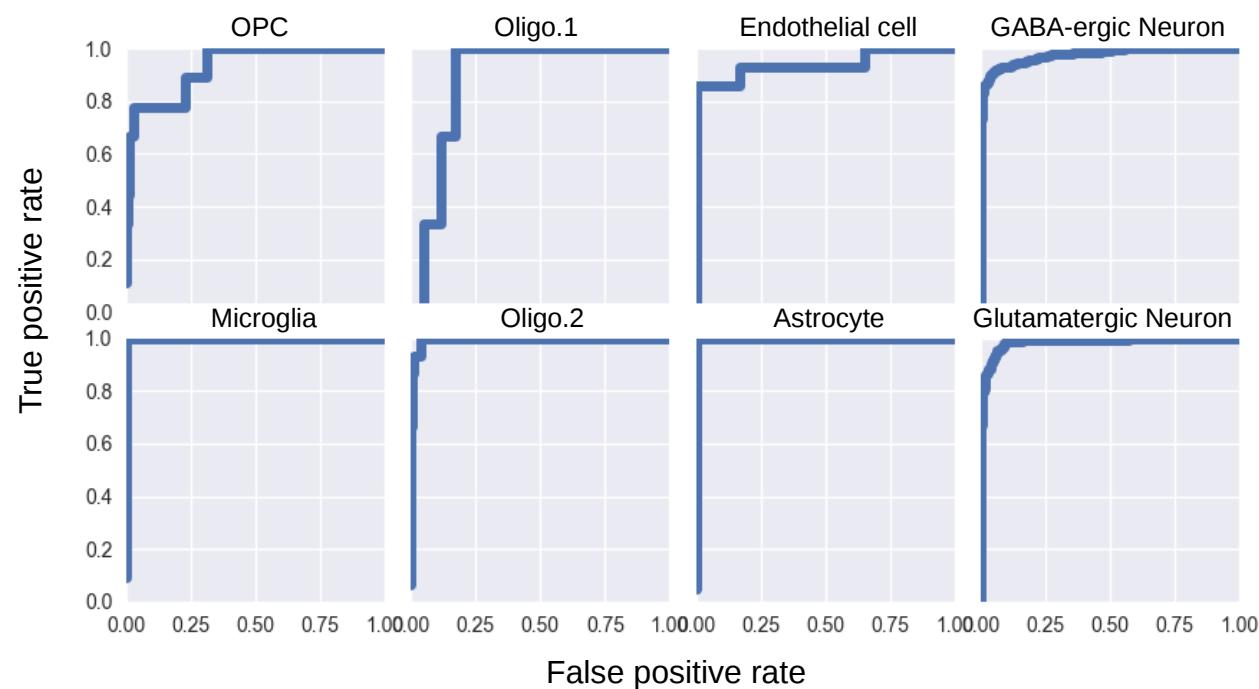


d

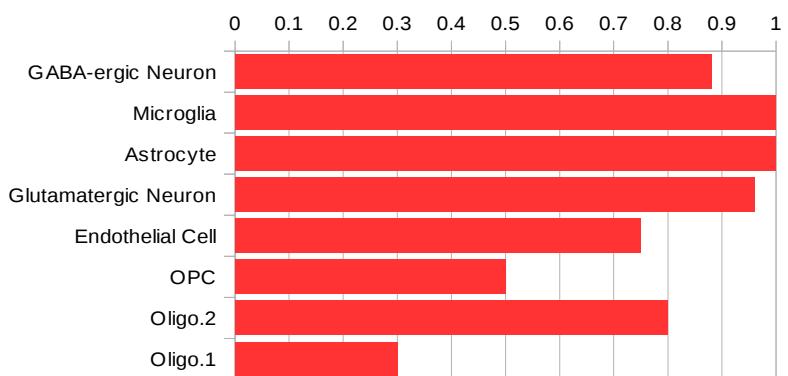


SFig 22

a



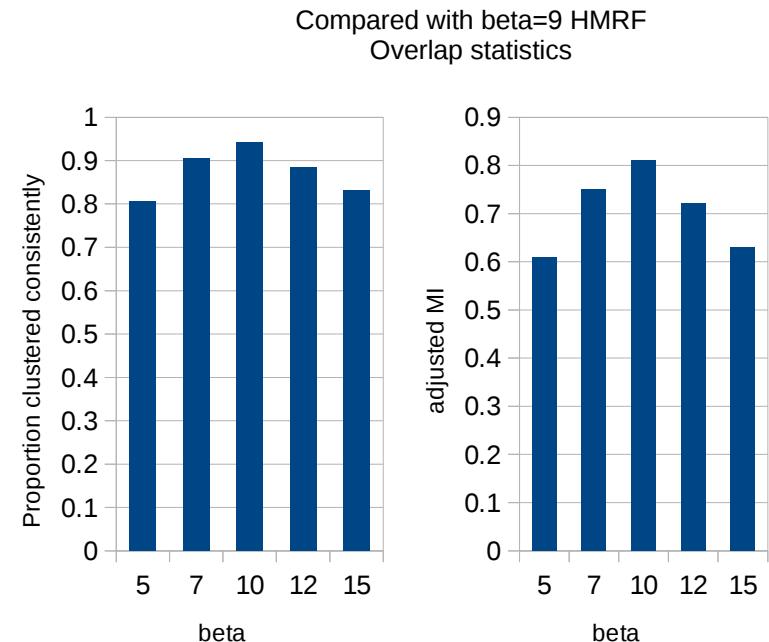
b



SFig 23



SFig 24

**a****b**

Compared with beta=9 HMRF  
Overlap matrices

0	1	2	3	4	5	6	7	8
116	0	0	0	0	2	0	7	2
0	135	0	2	0	36	14	0	1
1	2	106	0	0	15	13	12	3
0	7	1	104	0	14	32	1	1
1	0	0	0	82	0	5	0	0
0	10	1	1	0	270	47	0	2
0	7	3	2	0	23	156	1	4
3	1	7	1	0	28	4	161	3
0	3	2	1	0	10	12	0	119

0	1	2	3	4	5	6	7	8
116	0	0	0	0	1	0	5	0
0	136	0	2	0	3	7	0	0
1	2	108	0	0	2	5	5	0
0	6	0	102	0	4	20	1	0
1	0	0	0	82	0	0	4	0
2	12	0	5	0	36	37	0	17
0	6	2	0	0	12	201	0	1
1	0	8	1	0	3	0	174	0
0	3	2	1	0	4	8	0	117

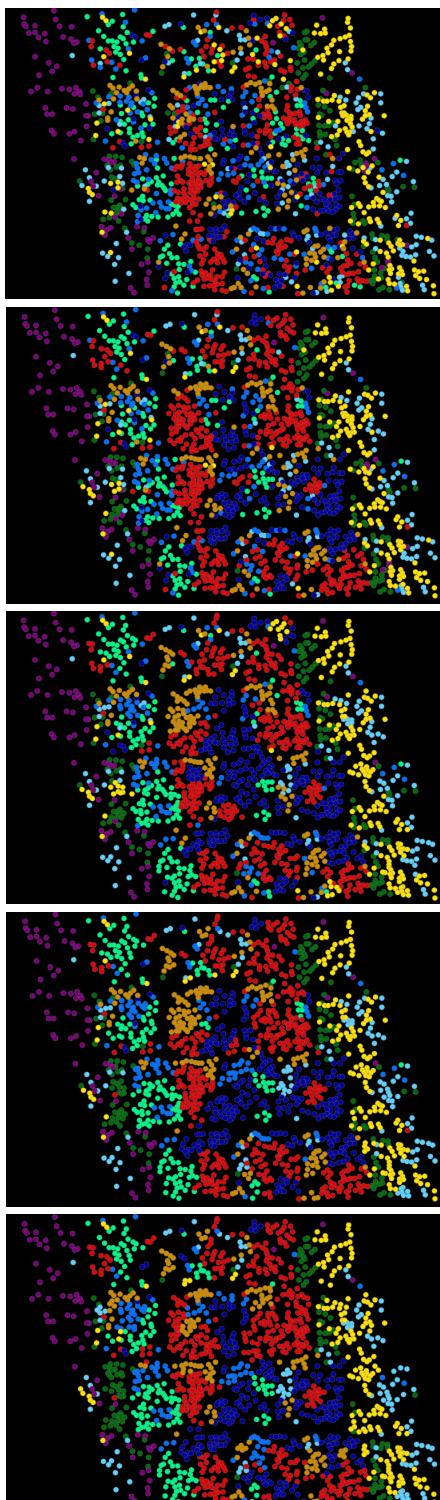
0	1	2	3	4	5	6	7	8
114	0	0	0	0	0	0	1	0
0	149	0	6	0	5	3	0	0
0	0	112	0	0	0	0	7	0
0	1	0	97	0	1	6	0	1
0	0	0	0	79	0	0	0	0
0	9	2	5	0	34	5	1	1
0	4	0	2	0	12	282	0	4
4	1	3	0	3	19	0	176	0
3	1	3	1	0	19	2	2	129

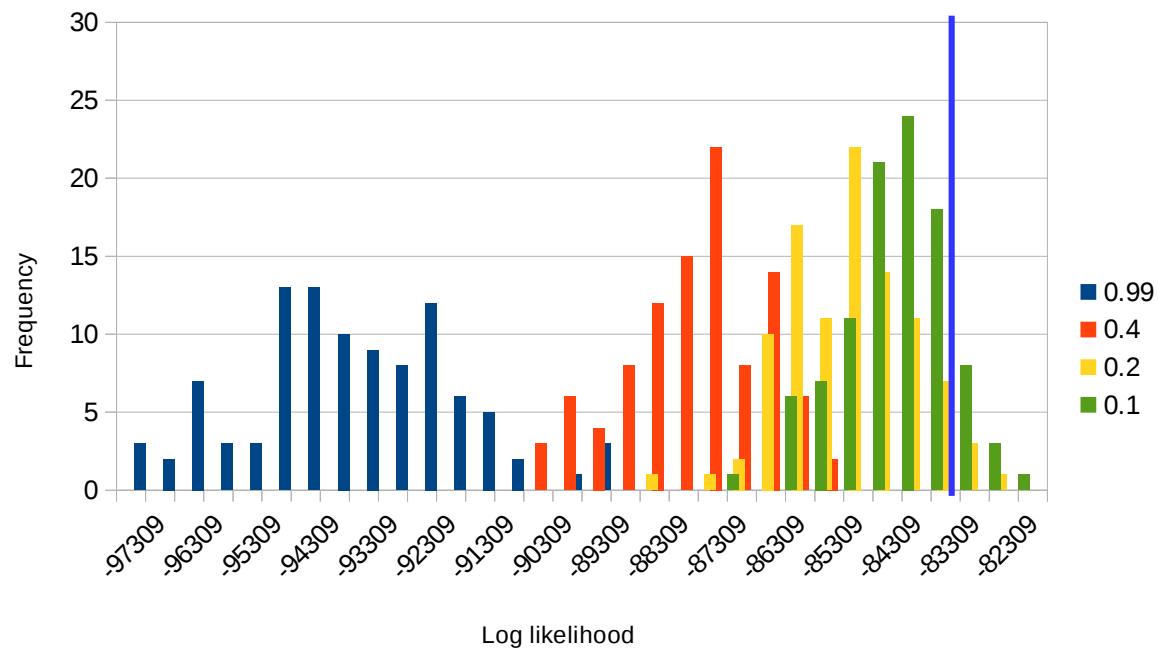
0	1	2	3	4	5	6	7	8
111	0	2	0	3	0	0	4	0
0	146	2	12	0	12	7	3	1
2	0	104	1	0	2	0	16	1
1	2	2	77	0	0	18	0	0
0	0	0	0	77	0	0	0	0
0	8	3	10	0	35	23	2	4
0	5	0	3	0	13	28	1	11
4	1	5	0	2	2	0	158	0
3	3	2	8	0	17	1	3	118

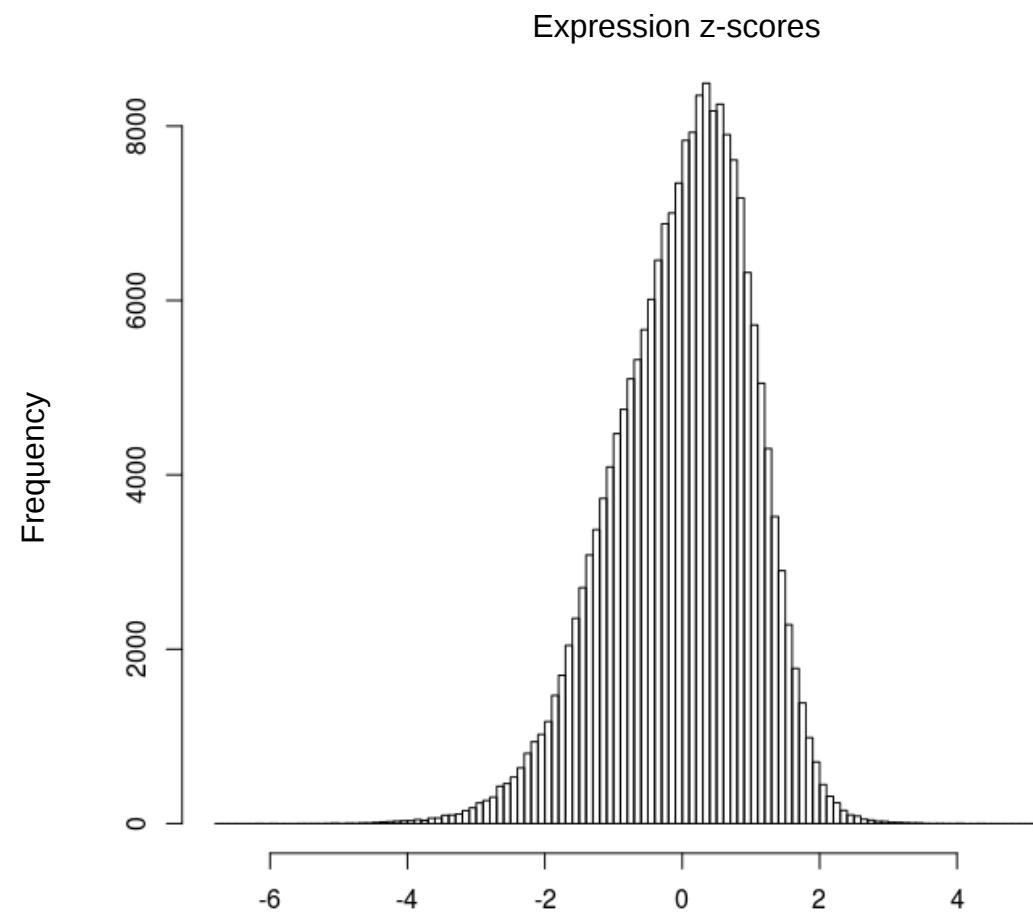
0	1	2	3	4	5	6	7	8
101	0	5	0	6	0	0	6	0
0	137	1	11	0	6	7	2	1
3	1	91	3	0	2	0	16	2
1	6	3	68	0	4	25	0	1
0	0	0	0	72	0	0	0	0
3	13	3	15	0	35	34	2	18
0	5	0	6	0	23	203	1	6
10	1	12	0	4	1	0	157	0
3	2	5	8	0	11	9	3	107

**c**

SFig 25



SFig 26



SFig 27

## Mann Whitney U test

